Chapter 17
Ill Health Effects of Food Lipids: Consequences of Inadequate Food Processing, Storage and Cooking

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Key Points

- The effect of nutrition on human health has received tremendous attention and traditional medical teaching that diet and nutrients play only limited roles in human health is being revised.
- Toxic products of food oxidation during food processing, storage, and cooking are the major determinants of the detrimental effects of various foods on human health.
- Flavor is the trait responsible for consumer preferences for meat and meat products while lipid oxidation during prolonged storage or short-term exposure to high temperatures is often associated with off-flavors.
- Lipid oxidation is a major problem in the storage of fatty foods affecting its quality and safety. Changing flavor, color, and texture results in significant generation of cytotoxic and genotoxic compounds and co-oxidizes many vitamins so that improvement of conditions of food processing, storage, and cooking is a frontline of future research.

Keywords Lipids · Health · Food · Antioxidants · Cooking

1 Introduction

The effect of nutrition on human health has received tremendous attention and traditional medical teaching that diet and nutrients play only limited roles in human health is being revised. In most developed countries nutritional practice has changed the focus from combating nutrient deficiencies to addressing nutrient requirements for maintaining good health throughout life.

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Chronic multifactorial diet-related diseases such as coronary heart disease (CHD), stroke, obesity, and diabetes mellitus are the major causes of mortality and morbidity worldwide, in particular in western countries. On average cardiovascular diseases (CVD, which include CHD and stroke) account for 38% of total deaths in the United States. The ratios of cardiovascular to total mortality varies from about 35 to 60% between western and eastern Europe [1]. Collectively, cardiovascular disease (including stroke), cancer, and diabetes account for approximately two-thirds of all deaths in the United States and about $700 billion in direct and indirect economic costs each year [2]. They account for nearly two of every three deaths in the United States—close to 1.5 million people in 2001 [3–5]. There is a range of different diets promoted in various countries by dieticians but, generally speaking, three major principles of healthy nutrition include variety, moderation and physical exercise. They are interlinked and ignorance of any of those causes health – related problems. Unfortunately in a modern society none of those principles are well followed. Considering improvement of the diet it is necessary to make sure that all nutrients in the diet are in optimal amounts and well protected against oxidation. It is believed that the amount and composition of fat in the diet is an important determinant of the pathobiology of many of these conditions. In particular, the relationship between dietary fats and CHD has been extensively studied with evidence emerging from cell culture experiments, animal studies, and observational and intervention studies in humans, indicating that dietary fat concentration and composition are important determinants of disease pathology [1]. However, it seems likely that toxic products of food oxidation during food processing, storage, and cooking are the major determinants of the detrimental effects of various foods on human health. Several types of diseases may be related to the exposure of humans to food-borne breakdown products of heated oils and cooked meat including atherosclerosis, the forerunner to cardiovascular disease; inflammatory joint disease, including rheumatoid arthritis; pathogenic conditions of the digestive tract; mutagenicity and genotoxicity, properties that often signal carcinogenesis; and teratogenicity, the property of chemicals that leads to the development of birth defects [6]. Indeed, the initial step for atherosclerosis development, leading to heart disease and stroke, is thought to be associated with oxidized LDL. Oxidized bases in DNA are potentially mutagenic and so are implicated in the process of carcinogenesis. Diabetes mellitus is also associated with oxidative damage to biomolecules [7]. Recently, the relation between dietary patterns and risk of cardiovascular, cancer, and all-cause mortality among 72,113 women who were free of myocardial infarction, angina, coronary artery surgery, stroke, diabetes mellitus, or cancer and were followed up from 1984 to 2002 has been evaluated [8]. Two major dietary patterns were identified: High prudent pattern scores represented high intakes of vegetables, fruit, legumes, fish, poultry, and whole grains, whereas high western pattern scores reflected high intakes of red meat, processed meat, refined grains, french fries, and sweets/desserts. After multivariable adjustment, the prudent diet was associated with a 28% lower risk of cardiovascular mortality and a 17% lower risk of all-cause mortality when the highest quintile was compared with the lowest quintile. In contrast, the western pattern was associated with a higher risk of mortality from cardiovascular disease, cancer, and all causes.

Flavor is the trait responsible for consumer preferences for meat and meat products. Water-soluble compounds in the lean portion of muscle impart meat taste while the lipids contribute the meat flavors [9]. Lipid oxidation during prolonged storage or short-term exposure to high temperatures is often associated with “off-flavors,” “warmed over flavor,” “rancid,” and “stale” characteristics in meat which result in product degradation and reduced case-life of an otherwise nutritious protein source. Lipid oxidation has been long recognized as a major problem in the storage of fatty foods affecting its quality and safety. First, it is a process responsible for changes

in flavor, color, and texture. Second, the oxidation of unsaturated lipids results in significant generation of cytotoxic and genotoxic compounds. Third, the free radicals generated by the process co-oxidize many vitamins, including vitamins A, E, C, and carotenoids and impair the nutritional quality of the foods [10]. It is necessary to take into account that oxidation of fatty acids in animal tissue starts to occur almost instantly after slaughter and various postmortem factors can influence lipid oxidation and decrease the shelf life of meat products due to the initiation of peroxidation. Therefore, improvement of conditions of food processing, storage, and cooking is a frontline of future research.

2 Free Radicals and Reactive Oxygen and Nitrogen Species

Free radicals are atoms or molecules containing one or more unpaired electrons. Free radicals are highly unstable and reactive and are capable of damaging biologically relevant molecules such as DNA, proteins, lipids, or carbohydrates. The animal body is under constant attack from free radicals, formed as a natural consequence of the body's normal metabolic activity and as part of the immune system's strategy for destroying invading microorganisms. Recently, collective terms such as reactive oxygen species (ROS) and reactive nitrogen species (RNS) have been introduced [11], including not only the oxygen or nitrogen radicals but also some nonradical reactive derivatives of oxygen and nitrogen.

Superoxide (O_2^{*-}) is the main free radical produced in biological systems during normal respiration in mitochondria and by autoxidation reactions with half-life at 37°C in the range of 1×10^{-6} s. Superoxide can inactivate some enzymes due to formation of unstable complexes with transition metals of enzyme prosthetic groups, followed by oxidative self-destruction of the active site [12]. Depending on condition, superoxide can act as oxidizing or a reducing agent. It is necessary to mention that superoxide, by itself, is not extremely dangerous and does not rapidly cross lipid membrane bilayer [13]. However, superoxide is a precursor of other, more powerful ROS. For example, it reacts with nitric oxide with a formation of peroxynitrite ($ONOO^-$), a strong oxidant, which leads to the formation of reactive intermediates due to spontaneous decomposition [14, 15]. In fact, $ONOO^-$ was shown to damage a wide variety of biomolecules, including proteins (via nitration of tyrosine or tryptophan residues or oxidation of methionine or selenocysteine residues), DNA, and lipids [16]. Superoxide can also participate in the production of more powerful radicals by donating an electron, and thereby reducing Fe^{3+} and Cu^{2+} to Fe^{2+} and Cu^+, as follows:

$$O_2^- + Fe^{3+}/Cu^{2+} \rightarrow Fe^{2+}/Cu^+ + O_2$$

Further reactions of Fe^{2+} and Cu^+ with H_2O_2 are a source of the hydroxyl radical ($^*OH$) in the Fenton reaction:

$$H_2O_2 + Fe^{2+}/Cu^+ \rightarrow {}^*OH + OH^- + Fe^{3+}/Cu^{2+}$$

The sum of reaction of superoxide radical with transition metals and transition metals with hydrogen peroxide is known as the Haber–Weiss reaction. It is necessary to underline that

superoxide radical is a "double-edged sword." It is beneficial when produced by activated polymorphonuclear leukocytes and other phagocytes as an essential component of their bactericidal activities but in excess it may result in tissue damage associated with inflammation.

Hydroxyl radical is the most reactive species with an estimated half-life of only about 10^{-9} s. It can damage any biological molecule it touches; however, its diffusion capability is restricted to only about two molecular diameters before reacting [17]. Therefore, in most cases, damaging effect of hydroxyl radical is restricted to the site of its formation. In general, hydroxyl radical can be generated in human/animal body as a result of radiation exposure from natural sources (radon gas, cosmic radiation) and from man-made sources (electromagnetic radiation and radionuclide contamination). In fact, in many cases hydroxyl radical is a trigger of chain reaction in lipid peroxidation.

Therefore, ROS/RNS are constantly produced in vivo in the course of the physiological metabolism in tissues. It is generally accepted that the electron-transport chain in the mitochondria is responsible for a major part of superoxide production in the body [11]. Mitochondrial electron transport system consumes more than 85% of all oxygen used by the cell and, because the efficiency of electron transport is not 100%, about 1–3% of electrons escape from the chain and the univalent reduction of molecular oxygen results in superoxide anion formation [18–20]. About 10^{12} O_2 molecules processed by each rat cell daily and if the leakage of partially reduced oxygen molecules is about 2%, this will yield about 2×10^{10} molecules of ROS per cell per day [21]. An interesting calculation has been made by Halliwell [18], showing that in the human body about 1.72 kg/year of superoxide radical is produced. In stress condition it would be substantially increased. Clearly, these calculations showed that free radical production in the body is substantial and many thousand biological molecules can be easily damaged if they are not protected. Recently, the role of mitochondria as a permanent source of ROS has been questioned [22].

The most important effect of free radicals on the cellular metabolism is due to their participation in lipid peroxidation reactions. The first step of this process is called the initiation phase, during which carbon-centered free radicals are produced from a precursor molecule, for example, a polyunsaturated fatty acid (PUFA):

$$\mathrm{LH} \xrightarrow{\text{Initiator}} \mathrm{L}*$$

The initiator in this reaction could by the hydroxyl radical, radiation, or some other events or compounds. In presence of oxygen these radicals (L^*) react with oxygen-producing peroxyl radicals starting the next stage of lipid peroxidation called the propagation phase:

$$\mathrm{L}* + \mathrm{O_2} \rightarrow \mathrm{LOO}*$$

At this stage, a relatively unreactive carbon-centered radical (L^*) is converted to a highly reactive peroxyl radical. A resulted peroxyl radical can attack any available peroxidizable material producing hydroperoxide (LOOH) and new carbon-centered radical (L^*):

$$\mathrm{LOO}* + \mathrm{LH} \rightarrow \mathrm{LOOH} + \mathrm{L}*$$

Therefore, lipid peroxidation is a chain reaction and potentially large number of cycles of peroxidation could cause substantial damage to cells. In membranes, the peroxidizable material is

represented by PUFAs. It is generally accepted that PUFA susceptibility to peroxidation is proportional to the amount of double bonds in the molecules. In fact, docosahexaenoic acid (DHA, 22:6*n*–3) and arachidonic acid (AA, 20:4*n*–6) are among major substrates of the peroxidation in the membrane. It is necessary to underline that the same PUFAs are responsible for maintenance of physiologically important membrane properties including fluidity and permeability. Therefore, as a result of lipid peroxidation within the biological membranes their structure and functions are compromised. Proteins and DNA are also important targets for ROS.

The complex structure of proteins and a variety of oxidizable functional groups of the amino acids make them susceptible to oxidative damage. In fact, the accumulation of oxidized proteins has been implicated in the aging process and in other age-related pathologies. A range of oxidized proteins and amino acids has been characterized in biological systems [23, 24]. In general the accumulation of oxidized proteins depends on the balance between antioxidants, prooxidants, and removal/repair mechanisms. Oxidation of proteins leads to the formation of reversible disulfide bridges. More severe protein oxidation causes a formation of chemically modified derivatives, e.g., Schiff's base [25]. Nitric oxide, hydroxyl radical, alkoxyl, and peroxyl radicals as well as carbon-centered radicals, hydrogen peroxide, aldehydes or other products of lipid peroxidation can attack protein molecules. Usually, oxidative modification of proteins occurs by two different mechanisms: a site-specific formation of ROS via redox-active transition metals and nonmetal-dependent ROS-induced oxidation of amino acids [25]. The modification of a protein occurs by either a direct oxidation of a specific amino acid in the protein molecule or cleavage of the protein backbone. In both cases, biological activity of the modified proteins would be compromised. The degree of protein damage depends on many different factors [26]:

- the nature and relative location of the oxidant or free radical source;
- nature and structure of protein;
- the proximity of ROS to protein target;
- the nature and concentrations of available antioxidants.

Normally, there is a delicate balance between the amount of free radicals generated in the body and the antioxidants to protect against them. For the majority of organisms on Earth, life without oxygen is impossible, animals, plants, and many micro-organisms rely on oxygen for the efficient production of energy. However, they pay a high price for pleasure of living in an oxygenated atmosphere since high oxygen concentration in the atmosphere is potentially toxic for living organisms.

Formation of ROS in foods during storage, processing, and cooking is closely interrelated among ROS. The most important ROS are hydroxy radical and singlet oxygen. Hydrogen peroxide and superoxide anion are important precursors for hydroxyl radical and singlet oxygen formation. It is extremely important to control the formation of ROS in foods to improve the food quality [27].

3 Three Levels of Antioxidant Defense

During evolution, living organisms have developed specific antioxidant protective mechanisms to deal with ROS and RNS [11]. Therefore, it is only the presence of natural antioxidants in living

organisms, which enable them to survive in an oxygen-rich environment [18]. These mechanisms are described by the general term "antioxidant system." It is diverse and responsible for the protection of cells from the actions of free radicals. This system includes

- Natural fat-soluble antioxidants (vitamins A, E, carotenoids, ubiquinones, etc.);
- Water-soluble antioxidants (ascorbic acid, uric acid, taurine, etc.);
- Antioxidant enzymes: glutathione peroxidase (GSH-Px), catalase (CAT), and superoxide dismutase (SOD);
- Thiol redox system consisting of the glutathione system (glutathione/glutathione reductase/glutaredoxin/glutathione peroxidase) and a thioredoxin system (thioredoxin/thioredoxin peroxidase/thioredoxin reductase).

The protective antioxidant compounds are located in organelles, subcellular compartments, or the extracellular space enabling maximum cellular protection to occur. Thus, antioxidant system of the living cell includes three major levels of defense [28–31]:

The first level of defense is responsible for prevention of free radical formation by removing precursors of free radicals or by inactivating catalysts and consists of three antioxidant enzymes namely SOD, GSH-Px, and CAT plus metal-binding proteins. Since the superoxide radical is the main free radical produced in physiological conditions in the cell [18] superoxide dismutase (EC 1.15.1.1) is considered to be the main element of the first level of antioxidant defense in the cell [29]. This enzyme dismutates the superoxide radical in the following reaction:

$$2O_2^* + 2H^+ \rightarrow H_2O_2 + O_2$$

The hydrogen peroxide formed by SOD action can be detoxified by GSH-Px or CAT which reduce it to water as follows:

$$H_2O_2 + 2GSH \rightarrow GSSG + 2H_2O$$

$$2H_2O_2 \rightarrow 2H_2O + O_2$$

Transition metal ions also accelerate the decomposition of lipid hydroperoxides into cytotoxic products such as aldehydes, alkoxyl radicals, and peroxyl radicals:

$$LOOH + Fe^{2+} \rightarrow LO^* + Fe^{3+} + OH^-$$

$$LOOH + Fe^{3+} \rightarrow LOO^* + Fe^{2+} + H^+$$

Therefore, metal-binding proteins (transferrin, lactoferrin, haptoglobin, hemopexin, metallothionein, ceruloplasmin, ferritin, albumin, myoglobin, etc.) also belong to the first level of defense. It is necessary to take into account that iron and copper are powerful promoters of free radical reactions and therefore their availability in "catalytic" forms is carefully regulated in vivo [32]. Therefore, organisms have evolved to keep transition metal ions safely sequestered in storage or transport proteins. In this way, the metal-binding proteins prevent formation of hydroxyl

radical by preventing them from participation in radical reactions. For example, transferrin binds the iron (about 0.1% of the total-body reserves), transports it in the plasma pool, and attaches it to the transferrin receptor. The important point is that iron associated with transferrin will not catalyze free radical reaction. Ferritin is considered to be involved in iron storage (about 30% of the total-body reserves) within the cytosol in various tissues including liver and spleen. Major part of iron in the body (55–60%) is associated with hemoglobin within red cells and about 10% with myoglobin in muscles [33]. A range of other iron-containing proteins (mainly enzymes) can be found in the body, including NADH dehydrogenase, cytochrome P450, ribonucleotide reductase, proline hydroxylase, tyrosine hydroxylase, peroxidases, catalase, cyclooxygenase, aconitase, succinate dehydrogenase, etc. [33]. Despite an importance of iron in various biochemical reactions, iron can be extremely dangerous when not carefully handled by proteins. In fact, in many stress conditions a release of free iron from its normal sites and its participation in Fenton chemistry mediate damages to cells. For example, superoxide radical can release iron from ferritin and H_2O_2 degrades the heme of hemoglobin to liberate iron ions [34].

Unfortunately, this first level of antioxidant defense in the cell is not sufficient to completely prevent free radical formation and some radicals do escape through the preventive first level of antioxidant safety screen initiating lipid peroxidation and causing damage to DNA and proteins. Therefore, the second level of defense consists of chain-breaking antioxidants—vitamin E, ubiquinol, carotenoids, vitamin A, ascorbic acid, uric acid, and some other antioxidants. Glutathione and thioredoxin systems also have a substantial role in the second level of antioxidant defense. Chain-breaking antioxidants inhibit peroxidation by keeping the chain length of the propagation reaction as small as possible. Therefore, they prevent the propagation step of lipid peroxidation by scavenging peroxyl radical intermediates in the chain reaction:

$$\mathrm{LOO^{*}} + \mathrm{Toc} \rightarrow \mathrm{Toc^{*}} + \mathrm{LOOH}$$

(LOO* is lipid peroxyl radical; Toc – tocopherol, Toc* – tocopheroxyl radical, LOOH – lipid hydroperoxide)

Vitamin E, the most effective natural free radical scavenger identified to date, is the main chain-breaking antioxidant in the cell. However, hydroperoxides, produced in the reaction of vitamin E with the peroxyl radical, are toxic and if not removed impair membrane structure and functions. In fact, lipid hydroperoxides are not stable and in the presence of transition metal ions can decompose producing new free radicals and cytotoxic aldehydes [35]. Therefore, hydroperoxides have to be removed from the cell in the same way as H_2O_2, but catalase is not able to detoxify these compounds and only Se-dependent GSH-Px can deal with them converting hydroperoxides into nonreactive products [36] as follows:

$$\mathrm{ROOH} + 2\mathrm{GSH} \rightarrow \mathrm{ROH(nontoxic)} + \mathrm{H_2O} + \mathrm{GSSG}$$

Thus, vitamin E performs only half the job in preventing lipid peroxidation by scavenging free radicals and forming hydroperoxides. The second part of this important process of antioxidant defense is due to Se-GSH-Px. It is necessary to underline that vitamin E and selenium work in a tandem; and even very high doses of dietary vitamin E cannot replace Se which is needed (in the form of GSH-Px and thioredoxin reductase) to complete the second part of antioxidant defense as mentioned above. Thus, Se as an integral part of the GSH-Px and thioredoxin reductase belongs to the first and second levels of antioxidant defense.

Coenzyme Q is considered to be an important antioxidant, which is synthesized in vivo (see Chapter 28), and is an important integral part of the antioxidant defense system in the cell.

Carotenoids recently were included into the family of natural antioxidants. They exhibit their maximum antioxidant activity at low oxygen pressures, which prevail in healthy tissues. It has been recently hypothesized that carotenoids are not the major antioxidant players themselves but rather are an important part of the antioxidant system [30]. Therefore, antioxidant interactions including their recycling provide an effective and reliable system of defense from free radicals and toxic products of their metabolism.

Vitamin C is a hydrophilic antioxidant functioning in an aqueous environment and possessing high free radical-scavenging activity [17]. It directly reacts with O_2^- and OH* and various lipid hydroperoxides and is taking part in the vitamin E recycling [17, 37]. Ascorbic acid is protective against a number of ROS [37–39].

Glutathione (GSH) is the most abundant nonprotein thiol in avian and mammalian cells and considered to be an active antioxidant in biological systems providing cells with their reducing milieu [40]. Cellular GSH plays a key role in many biological processes [41, 42].

Therefore, a crucial role for GSH is as a free radical scavenger, particularly effective against the hydroxyl radical [43], since there are no enzymatic defenses against this species of radical. Usually, decreased GSH concentration in tissues is associated with increased lipid peroxidation [44]. Furthermore in stress conditions, GSH prevents the loss of protein thiols and vitamin E [45] and plays an important role as a key modulator of cell signaling [46]. Animals and humans are able to synthesize glutathione. Uric acid is traditionally considered to be a metabolically inert end product of purine metabolism in man, without any physiological value. However, this ubiquitous compound has proven to be a selective antioxidant [47, 48].

However, even the second level of antioxidant defense in the cell is not able to prevent damaging effects of ROS and RNS on lipids, proteins, and DNA. In this case, the third level of defense is based on systems that eliminate damaged molecules or repair them. This level of antioxidant defense includes lipolytic (lipases), proteolytic (peptidases or proteases), and other enzymes (DNA repair enzymes, ligases, nucleases, polymerases, proteinases, phospholipases, and various transferases).

In spite of important roles of protein oxidation in pathogenesis of the development of various diseases, mechanisms for the control of protein oxidation and their repair have not been well studied and this has been a topic of great interest for the last few years. The oxidative damage to proteins is associated with alteration of transport proteins and ion dis-balance, disruption to the receptors and impair signal transduction, enzyme inactivation, etc. It is believed that conversion of –SH groups into disulfides and other oxidized species (e.g., oxyradicals) is one of the earliest events during the radical-mediated oxidation of proteins. Therefore, thioredoxin plus thioredoxin reductase deal with these changes by reducing protein disulfides to thiols and regulating redox-sensitive transcription factors [24]. The role of protein oxidation in food quality deterioration is still the subject of active discussion. For example, rainbow trout fillets were stored for 13 months at –20, –30, or –80°C, and samples were analyzed at regular intervals for lipid and protein oxidation markers. Detection of protein oxidation using immunoblotting revealed that high molecular weight proteins were oxidized already at $t = 0$ and that no new protein oxidized during storage, irrespective of the storage time and temperature [49].

It is interesting that reversible oxidation of cysteine could be an important cellular redox sensor in some proteins [50]. Methionine residues in proteins are also very susceptible to oxidation with methionine sulfoxide formation, which was detected in native proteins [51]. This could affect activity of various proteins. In fact, almost all forms of ROS oxidize methionine residues of proteins to a mixture of the *R*- and *S*-isomers of methionine sulfoxide [52]. Methionine sulfoxide reductase (Msr) can reduce either the free or the protein-bound methionine sulfoxide back to methionine. Therefore, Msr is considered a repair mechanism for dealing with the product of reaction of oxidants with methionine residues [53]. The authors hypothesized that methionine residues function as a "last chance" antioxidant defense system for proteins. It was shown that in bacterial glutamine synthetase surface-exposed methionine residues surrounding the entrance to the active site are preferentially oxidized and other residues (e.g., cystein) within the critical regions of the protein are protected without loss of catalytic activity of the protein [53]. Indeed, due to Msr activity the methionine–methionine sulfoxide pair can function catalytically. MsrA is present in most living organisms and is encoded by a single gene and the mammalian enzyme has been detected in all tissues studied. In particular it is found in the cytosol and mitochondria of rat liver cells [54]. Msr is considered to have at least three important functions in cellular metabolism including antioxidant defense, repair enzyme, and a regulator of certain enzyme function and possibly participation in signal transduction [52, 55].

MsrA has been known for a long time, and its repairing function is well characterized; however, recently, a new methionine sulfoxide reductase was characterized [56]. It was referred to as MsrB and it was shown that the gene of MsrB is present in genomes of eubacteria, archaebacteria, and eukaryotes. Therefore, in mammals two methionine sulfoxide reductases, MsrA and MsrB, are expressed with different substrate specificity [56]. They catalyze the thioredoxin-dependent reduction of the *S*-isomer and *R*-isomer of methionine sulfoxide to methionine.

Recently, the major mammalian MsrB has been identified as a selenoprotein [57, 58]. In fact it has been found that selenoprotein R is a zinc-containing stereo-specific Msr [58]. Moreover, Se deficiency in a mouse was associated with a substantial decrease in the levels of MsrB-catalytic activity, MsrB protein, and MsrB mRNA in liver and kidney tissues [59]. It has been reported that human and mouse genomes possess three MsrB genes responsible for synthesis of the following protein products: MsrB1, MsrB2, and MsrB3 [60]. In particular, MsrB1 (Selenoprotein R) was present in the cytosol and nucleus and exhibited the highest methionine-*R*-sulfoxide reductase activity due to the presence of selenocysteine (Sec) in its active site. Other mammalian MsrBs are not selenoproteins and contain cysteine in place of Sec and were less catalytically efficient [60, 61].

All these antioxidants are operating in the body in association with each other forming an integrated antioxidant system. The cooperative interactions between antioxidants in the cell are vital for maximum protection from the deleterious effects of free radicals and toxic products of their metabolism. For example, it is well established that vitamin E is the major antioxidant in biological membranes, a "head quarter" of antioxidant network. However, it is usually present there in low molar ratios (one molecule per 2000–3000 phospholipids) but vitamin E deficiency is difficult to induce in adult animals. It is probably due to the fact that oxidized vitamin E can be converted back into the active reduced form by reacting with other antioxidants: ascorbic acid, glutathione, ubiquinols, or carotenoids. A connection of antioxidant defense to the general body metabolism (the pentose phosphate cycle is the major producer of reducing equivalents in the form of NADPH) was demonstrated and involvement of other nutrients in this process was shown this process. For example, dietary protein is a source of essential amino acids for glutathione

synthesis, riboflavin is an essential part of glutathione reductase, niacin is a part of NADPH, and Se is an integral part of thioredoxin reductase. At the same time, thiamine is required for transketolase in the pentose phosphate pathway.

It is proven that the antioxidant protection in the cell not only depends on vitamin E concentration and location but also relies on the effective recycling. Indeed, if the recycling is effective then even low vitamin E concentrations are able to maintain high antioxidant protection in physiological conditions. For example, this could be demonstrated using chicken brain as a model system. Indeed, our data [30] indicate that the brain is characterized by extremely high concentrations of long-chain polyunsaturated fatty acids predisposing this tissue to lipid peroxidation. Furthermore, brain contains much lower levels of vitamin E than other body tissues. However, in fresh chicken brain, levels of products of lipid peroxidation are very low, which could be a reflection of an effective vitamin E recycling by ascorbic acid which is present in this tissue in comparatively high concentrations. Antioxidant recycling is the most important element in understanding mechanisms involved in antioxidant protection against oxidative stress. The rate of regeneration, or recycling, of the vitamin E radicals may affect both its antioxidant efficiency and its lifetime in biological systems.

As can be seen from data presented above the antioxidant defense includes several options [30, 31]:

- Decrease localized oxygen concentration;
- Prevention of first-chain initiation by scavenging initial radicals (SOD, GSH-Px, and catalase);
- Binding metal ions (metal-binding proteins);
- Decomposition of peroxides by converting them to nonradical, nontoxic products (Se-GSH-Px);
- Chain breaking by scavenging intermediate radicals such as peroxyl and alkoxyl radicals (vitamins E, C, glutathione, uric acid, ubiquinol, bilirubin, etc.);
- Repair and removal of damaged molecules.

4 Meat Consumption and Cancer

Most of the published literature on meat in relation to cancer development has focused on colorectal cancer (CRC). There have been some studies investigating possible associations between meat and other types of cancer, including gastric, breast, prostate, and kidney cancers and cancer of the pancreas; however, the evidence in relation to these other types of cancer has been found to be weak or inconsistent [62]. It is important to mention that CRC is the third most common cancer in the world. In the United States, the estimated new cancer cases for colon and rectum cancer in 2008 were approximately 108.1 and 40.7 thousands, respectively, and estimated death for CRC was about 50,000 people [63]. It is believed that 80% of cases of CRC are sporadic (i.e., arise spontaneously) and appear to be influenced by environmental and lifestyle factors, such as diet and physical activity level.

High meat intake has been associated with an increased risk of colon cancer in several studies. In particular, consumption of red meat related directly to the incidence of CRC [64]. However, the question whether red meat itself or oxidative products produced as a result of meat cooking

influences risk of CRC remains to be resolved. The relation between dietary factors and the risk of colorectal cancer was investigated in a case–control study conducted in Pordenone province, northeastern Italy, on 123 cases of colon cancer, 125 of rectal cancer, and 699 controls admitted to hospital for acute, non-neoplastic or digestive disorders [65]. Consistent positive associations CRC were observed with more frequent consumption of bread, pasta, polenta, cheese, eggs, and red meat. Risk of colon or rectal cancer was about twice as great among those who consumed these foods more frequently. Using data from a case–control study conducted between 1985 and 1992 in northern Italy on 828 cases of colon cancer, 498 cases of rectal cancer, and 2,024 controls in hospital were investigated [66]. In particular, it was shown that 17% of CRC cases were attributable to consumption of red meat. Recently, a case–control study was conducted to evaluate the interaction between red meat consumption and colorectal cancer incidence in Ontario, Canada [67]. Colorectal cancer cases diagnosed during 1997–2000 in people of 20–74 years of age, were identified. Controls were sex-matched and age group-matched random samples of the Ontario population. Epidemiologic and food questionnaires were completed by 1,095 cases and 1,890 controls; blood was provided by 842 and 1,251, respectively. Multivariate logistic regression was used to obtain adjusted odds ratio (OR) estimates. When comparison was made between people consuming >5 red meat servings per week and those consuming $\leq$2 servings/week, a 1.7-fold increased colorectal cancer risk was observed. Colorectal cancer risk also increased significantly with well-done meat intake. A case–control study of 146 cases of colorectal adenoma and 228 polyp-free controls was conducted [68]. It was shown that there was a twofold increased risk of CRC in the highest, compared with the lowest, quartile of processed meat intake.

Two meta-analyses on relationship between meat consumption and CRC incidence have been published. Thirteen studies were included in the first meta-analysis [69]. Pooled results indicated that a daily increase of 100 g of all meat or red meat was associated with a significant 12–17% increased risk of colorectal cancer. A significant 49% increased risk was found for a daily increase of 25 g of processed meat. Some studies have implicated red meat (including high-temperature cooked meats), whereas others have implicated processed meats. However, the second meta-analysis conducted by Norat et al. [70] found that total meat consumption was not significantly associated with risk of CRC, but that consumption of red meat and processed meat was associated with about a 33% greater risk of CRC.

Therefore, it seems likely that meat cooking is responsible for formation of by-products, which are involved in cancer promotion. It has been suggested that cancer results from the accumulation of multiple mutations in key growth regulatory genes [71]. These genetic changes are a consequence of the inherent chemical instability of DNA under physiological conditions, errors made by the DNA replication and maintenance machinery, and replication of DNA bases that are chemically modified as a result of exposure to exogenous or endogenous genotoxins [72]. The loss of genomic stability and resulting gene alterations are key molecular pathogenic steps that occur early in tumorigenesis; they permit the acquisition of a sufficient number of alterations in tumor suppressor genes and oncogenes that transform cells and promote tumor progression [73].

5 Lipid Peroxidation in Food and Its Consequences

The food, as a whole, is a particularly complex chemical matrix and lipid peroxidation is a leading cause of its quality deterioration. While in the raw foods the enzymatic oxidation plays a most significant role, in the processed foods, the chemical initiation (presence of free iron or

copper) is probably the main determinant of the process [74]. It is generally accepted that in modern food technology low-level oxidation of lipids in meat, poultry, and milk during storage and processing is practically unavoidable [75]. In fact, lipid stability in meat and meat products depends on many factors. They include

- species,
- muscle type,
- the amount and type of fat in the diet,
- the nutritional status of the animal at slaughter,
- the presence or absence of disease or infection, and
- the type of processing to which the meat is subjected [76].

It is generally accepted that most fried meat products contain lipid peroxides in various concentrations and if cooked meat is stored, the level of peroxidized PUFAs increases dramatically. For example, in heated turkey red muscle (a fast food) the level of lipid peroxides was found to be about 100-fold higher than in fresh turkey red meat [77] and this comprised only part of total lipid peroxides consumed every day. Fish and fish oil are especially susceptible to peroxidation due to presence of highly unsaturated docosahexaenoic (DHA, 22:6*n*–3), docosapentaenoic (DPA, 22:5*n*–3), and eicosapentaenoic (EPA, 20:5*n*–3) fatty acids.

Once a free radical is generated, the chain reaction of oxidation is initiated, new free radicals, carbon and oxygen centered, are formed and the process is easily propagated. The net chemical result of lipid oxidation is very complex. Lipid hydroperoxides (LOOH) derived from unsaturated fatty acids are important intermediates of peroxidative reactions induced by ROS. Lipid hydroperoxides are not stable and in the presence of transition metal ions can decompose producing new free radicals and cytotoxic aldehydes [35]. This decomposition proceeds by hemolytic cleavage of a peroxy bond to form alkoxy radicals and they undergo carbon–carbon cleavage to form breakdown products including aldehydes, ketones, alcohols, hydrocarbons, esters, furans, and lactones. Indeed, lipid oxidation yields a very complex group of by-products that contribute to the flavor deterioration of foods and implicated in biological oxidation and can cause oxidative stress [78]. It is interesting to mention that the oxidation products of fatty acids, the hydroperoxides usually are tasteless and are not responsible for the off-flavors. It is their shorter chain derivatives, i.e., the hydrocarbons, alcohols, ketones, and aldehydes which are responsible for the rancidity [27].

Oxidized lipids are partly absorbed in the digestive tract [79] and incorporated into membrane phospholipids altering their structure and properties [80]. For example, chylomicrons isolated from subjects consuming oxidized fat are more susceptible to lipid peroxidation ex vivo, suggesting that at least some oxidized fatty acids are absorbed [81]. In animal models it has been shown that oxidized lipids in the diet can suppress growth [82, 83], reduce vitamin E level in tissues increasing their susceptibility to lipid peroxidation [84], increase tissue protein oxidation [85], and increase the number of aberrant crypts in the intestine [85, 86]. In particular, in rats consuming thermally oxidized corn oil, increased concentrations of lipid peroxides were observed in the liver and kidney, in association with a decreased growth rate, food, and protein efficiency ratio [87, 88]. The gastrointestinal epithelium of swine and chickens responded to oxidant stress imposed by oxidized fat by increased enterocyte turnover and the gut associated immune system was compromised [89]. The consumption of oxidized fats is associated with

diarrhea, liver enlargement, growth depression, and histological changes in tissues of experimental animals [90–93]. Heated oils also showed potent teratogenic actions in experimental animals [94]. The genotoxicity of heated cooking oil vapors has been demonstrated [95]. In mice, the tumor-initiating activity of oil used repeatedly to fry fish has also been reported [96]. The presence of 4-oxo-2-hexenal (4-OHE) may partly explain these genotoxicity results. Indeed, 4-OHE was detected in the human diet and in cooking vapor [97]. It may be involved in cancer induction in the digestive tract, such as stomach, esophagus, and colon, because the 4-OHE-DNA adduct was detected in mouse digestive tract organs after oral administration.

Malondialdehyde (MDA) is an endogenous genotoxic product of enzymatic and oxygen radical-induced lipid peroxidation whose adducts are known to exist in DNA isolated from healthy human beings. MDA is mutagenic in bacterial and mammalian cell assays, and it is carcinogenic in rats [98]. Recently, the biological consequences of the replication of MDA-modified double-stranded DNA in human cells have been studied [72]. The study revealed that MDA-induced DNA damage is mutagenic; it also provided evidence for the occurrence of a previously undetected lesion that may be highly mutagenic. This lesion may contribute significantly to the genotoxicity associated with lipid peroxidation and oxidative stress. MDA is one of the most abundant lipid peroxidation cytotoxins formed in foods, especially in meat, or endogenously in vivo [10]. After ingestion of peroxidized foods, animals and humans have been shown to excrete an increased amount of MDA in the urine and recent results revealed a relatively rapid accumulation of MDA in plasma, with a maximum level achieved 3 h after the meal [99].

During the storage or cooking of foods, lipid peroxidation proceeds and is accelerated by heat, light, and transition metals. As secondary products, various electrophilic compounds, such as malondialdehyde and α,β-unsaturated aldehydes including acrolein, crotonaldehyde, and 4-hydroxynonenal (4-HNE), are formed [100]. They readily react with DNA and have mutagenic and genotoxic potential [101, 102]. In particular, 4-HNE is a product of omega-6 fat peroxidation and forms a cyclic 1,N^2-propano-deoxyguanosine adduct upon reaction with DNA [103]. 4-HNE is a strong alkylating agent reacting rapidly with proteins, an interaction resulting in the inhibition of DNA, RNA, and protein synthesis. Possibly connected with this effect is the observation that HNE inhibits cell proliferation and at concentrations >10 μM induces irreversible cellular damage. Besides, HNE was shown to induce significant amounts of DNA fragmentation, significant levels of sister chromatid exchanges, and a dose-dependent increase in the number of mutations to 6-thioguanine resistance [104]. Indeed, 4-HNE shows mutagenicity in V79 Chinese hamster lung cells [105] and in human cells [106]. A related compound, 4-oxo-2-nonenal (4-ONE), is also produced via 4-hydroperoxy-2-nonenal as a product of lipid peroxidation [107], and it forms adducts with deoxynucleosides and DNA [108]. The cyclic 1,N [2]-propanodeoxyguanosine adducts, derived from α,β-unsaturated aldehydes, including acrolein (Acr), crotonaldehyde (Cro), and *trans*-4-hydroxy-2-nonenal (HNE), have been detected as endogenous DNA lesions in rodent and human tissues. Collective evidence has indicated that the oxidative metabolism of PUFAs is an important pathway for endogenous formation of these adducts [109].

One of the biggest contributors to the consumption of lipid peroxides are fast foods, since the typical American consumes approximately three hamburgers and four servings of fries per week [110]. They could provide a significant amount of potentially hazardous peroxides as well as *trans*-fatty acids. The percentage of fat from fast foods and ethnic foods increased from 1% in 1965 to 11% in 1996 [111]. In particular oils, which are used for deep-fat frying (e.g., chips and

French fries preparation), are heated to very high temperature and decomposition products are formed [112]. In fact, most of the oxidized lipids in foods come from fats and oils heated at high temperature in particular from frying fats [111]. During frying, the oil undergoes three deleterious reactions: hydrolysis caused by water, oxidation, and thermal alteration caused by oxygen and heat [110]. These reactions cause the formation of polymerization products, of which over 400 have been identified [113]. Furthermore, decomposition products, which are formed as a result of reactions between food ingredients and oil, comprise another large group of potentially toxic compounds [114]. It is generally accepted that oxygen plays a major role in the deterioration of the oil during frying and selective absorption may occur, enriching the food product with breakdown oil compounds [110]. Products of lipid oxidation formed in the food depend on the temperature. For example, at low or moderate temperature hydroperoxides are the major products formed while in high-temperature-treated products secondary oxidized triacylglycerol monomers and polymers are more common compounds [111]. Therefore, food frying in fast-food restaurants may be problematic due to lengthy oil exposure to extreme conditions and the lack of adequate oil replenishment and discarding. In particular, a significant number of oils and fats from fast-food outlets contain more than 25% newly formed compounds [111].

Lipid peroxidation is associated with the formation of a wide range of secondary aldehyde products such as *n*-alkanals, *trans*-2-alkenals, 4-hydroxy-*trans*-2-alkenals, and MDA [115]. While linoleic, gamma-linolenic and arachidonic acids found in different foods were precursors of hexanal, propanal was the dominant aldehyde formed from the breakdown of alpha-linolenic, eicosapentaenoic, and docosahexaenoic acids [116]. For example, propional, pentenal, hexanal, and 4-hydroxynonenal were the primary aldehydes formed during lipid oxidation in beef [115]. Those products are shown to be comparatively stable and can readily diffuse into cells causing toxicological effects [117]. Therefore, prolonged frying caused a substantial rise in MDA concentration [110] which is shown to be toxic and mutagenic. Furthermore, MDA can damage proteins and phospholipids by covalent bonding and cross-linking [118]. Rats fed a diet containing MDA suffered from retarded growth, irregular intestinal activities, enlarged liver and kidneys, anemia, and low serum and liver vitamin E [119]. Similarly, the results of Raza et al. [120] showed that 4-hydroxynonenal (HNE), a reactive by-product of lipid peroxidation, caused mitochondrial oxidative stress leading to a decrease in the GSH pool and increased membrane lipid peroxidation.

It is necessary to underline that heat treatment of the food can also cause heterocyclic amine formation. For example, approximately 20 heterocyclic amines of high mutagenesis were isolated and identified from protein-rich foods [110]. Furthermore, mutagenic activity was found in beef cooked in regular domestic conditions [121]. It has been shown that heterocyclic amines can cause oxidative stress leading to DNA adduct formation and oxidative DNA damage [122]. Therefore, heterocyclic amines formed during the cooking of meat and fish and possessing mutagenic, genotoxic, and carcinogenic properties can be detected in burgers, steaks, pork ribs [123, 124].

Acrylamide in food products chiefly in commercially available potato chips, potato fries, cereals, and bread was determined by liquid chromatography-tandem mass spectrometry in 30 food samples [125]. Concentrations of acrylamide varied from 14 ng/g (bread) to 3700 ng/g (potato chips) and the WHO estimates the average consumer ingests about 0.8 μg/kg body weight daily [126]. It is necessary to take into account that acrylamide caused an increase in lipid peroxidation and decrease in glutathione contents and activity of glutathione-*S*-transferase in the rat liver in a dose-dependent manner [127].

The biggest killers of the modern society, cardiovascular diseases including atherosclerosis, may result at least partly from processes that occur after ingestion of high-fat foods that contain lipid oxidation end products, some of which are cytotoxic and genotoxic compounds such as oxycholesterol, 4-hydroxy-nonenal, and MDA [10, 99]. Evidence for a putative role of some of these compounds in accelerating events in the atherogenic process—the initiation of endothelial injury, the accumulation of plaque, and the termination phase of thrombosis—comes from both animal and human studies [128]. Therefore, products of oxidation of food could contribute to CVD and cancer development in various countries worldwide and prevention of food oxidation is an important task for food industry. However, in a recent UK study consumption of red or processed meat assessed separately was not related to the major risk factors for CHD [129]. Similarly, partial replacement of dietary carbohydrate with protein from lean red meat does not elevate oxidative stress or inflammation [130].

6 Antioxidants and Food Quality

For the last few years consumer demands regarding aspects of meat quality have substantially increased. Therefore, a challenge to the meat industry is to enhance the image of meat purchased at the supermarket [131]. There are many meat quality characteristics that attract consumer attention. They include appearance, texture, and flavor [132] as well as tenderness, juiciness, aroma [131], and other subjective characteristics. Among these, appearance has a major impact on the initial decision of the customer to purchase or reject the product [133]. Consumers prefer fresh meat with a minimum loss of water during handling and cooking. Therefore, water-holding capacity of the meat [134] as well as color [135] and absence off-flavors [133] are considered among most important meat quality characteristics.

It has been shown that sensory quality of meat is affected by muscle biochemistry and modern processing technologies [136]. For example, grinding increases oxygen incorporation into muscle and cooking releases protein-bound iron into the intracellular pool [137]. As shown above, in this process free radical production and lipid peroxidation cause membrane structure disruption, which leads ultimately to significant losses in food quality, including off-flavor, off-colors, poor texture, etc. [138].

One approach to enhancing oxidative stability of meat is to add antioxidants either into the animal diet or directly during processing [139]. For example, an increasing body of evidence indicates that increased vitamin E supplementation is an effective means of meat quality improvement in chickens, turkeys, cattle, pigs, and lambs [132, 133, 140, 141]. However, when a nutritional strategy for improving meat quality is developing it is necessary to take into account antioxidant interactions in the diet and in the cell. For example, synergism between Se and vitamin E could be used for further improvement of meat antioxidant status and decreasing lipid peroxidation during meat processing, storage, and cooking. In fact, it has been shown that GSH-Px activity in muscles did not change significantly over 8-day storage of beef [142]. This means that once GSH-Px activity is elevated it is maintained postmortem. Therefore, one might expect a stabilizing effect of dietary Se supplementation during meat storage. Indeed, supplementing broiler diets with 0.25 ppm Se substantially increased GSH-Px activity in breast (2.1-fold) and leg (4.1-fold) muscle, and as a result decreased lipid peroxidation was detected (2.5-fold in breast muscle and 3.3-fold in leg muscles) after 4 days storage at 4°C compared to the control group

[143]. These data clearly indicate that GSH-Px significantly contributes to the overall antioxidant defense of muscle, decreasing tissue susceptibility to lipid peroxidation and that increasing oxidative stability of skeletal muscle can be accomplished by organic Se supplementation of the diet. Protective effects of Se may be not direct, but are mediated via improvement of other chains of antioxidant defense. For example, Se in combination with vitamin E increased activity of SOD in chicken serum [144]. A stabilizing effect of Se in combination with other antioxidants on meat quality would be a great advantage in producing the so-called "designer" meat. For example, meat enriched with *n*–3 PUFAs was shown to have increased TBA values during storage; and the same meat from antioxidant-supplemented (Se + vitamins E and C) chickens showed lower TBA values and greater color stability during storage [145–147] inclusion of organic selenium in the chicken diet increased Se-GSH-Px activity in muscles more than twofold. A combination of organic selenium and vitamin E supplementation was associated with the highest Se-GSH-Px activity in muscles. The highest level of the final product of lipid peroxidation in muscle after 2-year storage at –20°C was found in muscles from chickens fed on a semi-synthetic diet and characterized by the lowest vitamin E and Se-GSH-Px activity. The lowest initial level of MDA was found in muscles from birds fed diets supplemented with either 200 ppm vitamin E or 100 ppm vitamin E in combination with 0.4 ppm organic selenium.

There is a great body of information indicating on one hand that adding other antioxidants into the animal diet is not as effective as vitamin E or Se and on the other hand, adding various plant extracts directly to the meat could be an effective approach to decrease lipid peroxidation and maintain meat quality. For example, supplementation of pig diets with green tea catechins is not associated with improved antioxidant status and meat quality under practice-oriented conditions [148]. Natural tocopherols (TC), rosemary (RO), green tea (GT), grape seed, and tomato extracts were supplemented in single and in combinations at total concentrations of 100 and 200 mg/kg of feed in a 4% linseed oil-containing diet to investigate the oxidative stability of broiler breast muscle [149]. The muscle alpha-tocopherol content linearly responded to the feed alpha-tocopherol content and thus there were no indications for a sparing effect on alpha-tocopherol from other antioxidant treatments. In summary, dietary natural antioxidant extracts were less effective than the treatment with synthetic antioxidants combined with alpha-tocopheryl acetate for protecting against oxidation. Thirty-six 12-week-old turkeys were distributed into six groups and were raised for 4 weeks on rations containing 0, 0.5, or 1.0% dehydrated rosemary leaves as antioxidants in the presence of alpha-tocopheryl acetate from 10 to 300 mg/kg [150]. No significant (p >0.05) changes could be observed in the alpha-tocopherol content of breast and thigh of turkeys consuming rations containing up to 1% dehydrated rosemary leaves. The refrigeration of the meats led to spontaneous increase in the MDA content of the breast and thigh meat samples. Samples from turkeys fed rations containing 300 mg/kg alpha-tocopheryl acetate showed the lowest mean levels of MDA after the 9-day refrigerated period. The incorporation of rosemary in the rations led to a modest decrease in the formation of MDA in the meats compared with the respective mean control values. The combination of alpha-tocopheryl acetate and rosemary was not associated with an additional decrease in MDA formation.

There were quite a few products tested as additives to processed meat. For example, inclusion of 3% dried plum puree was effective as a natural antioxidant for suppressing lipid oxidation in precooked pork sausage patties [151]. Similarly, grape seed extract was shown to be an effective antioxidant in ground chicken thigh meat that does not affect moisture content or pH during storage, inhibits TBARS formation, helps to mitigate the prooxidative effects of NaCl, and may alter the effect of NaCl on protein solubility in salted chicken patties [152]. Indeed, grape seed

extract at 0.02% has the potential to reduce oxidative rancidity and improve shelf life of refrigerated cooked beef and pork patties [153]. The antioxidant and antimicrobial effects of equivalent concentrations of fresh garlic (FG), garlic powder (GP), and garlic oil (GO) were investigated against lipid oxidation and microbial growth in raw chicken sausage during storage at 3°C [154]. Addition of either garlic or BHA (0.1 g/kg) significantly delayed lipid oxidation when compared with control. The results suggest that fresh garlic and garlic powder, through their combined antioxidant and antimicrobial effects, are potentially useful in preserving meat products.

7 Conclusions: Future Trends in Food Industry

From information presented above it is clear that in most cases producers and consumers themselves are responsible for increased levels of prooxidants in the diet and ultimately in the GIT. Therefore, there is a need for changes in ways our food is produced, prepared, stored, and eaten (Table 17.1). It is possible to improve the situation both at the producer and at the consumer levels.

Table 17. 1 Healthy meals via antioxidant enrichment and decreased lipid peroxidation (Adapted from Surai [31])

	Meat	Egg	Fish
Technological improvement at the producer level			
Vitamin E enrichment	+++	+++	+++
Selenium enrichment	+++	+++	+
Carotenoid enrichment	+	+++	+++
Food preparation			
Cooking oil	Olive	Olive	Olive
Boiling vs frying	+	+++	+
Spices and herbs	+++	+++	+++
Food serving			
With vegetables	+++	+++	+++
Meal composition			
Fruit	+++	+++	+++
Fruit juice	+++	+++	+++
Red wine	+++	+	+
Tea	+++	+++	+++

7.1 At the Producer Level

- To enrich meats and meat-related food with vitamin E. Indeed, there is a great body of information accumulated indicating that chicken [155], turkey [156, 157], pork [141], beef [132], lamb [158], as well as meat from other species [159] can be enriched with vitamin E and this technological solution can substantially decrease lipid peroxidation in meat during processing, storage, and cooking.
- To enrich meat with organic selenium. This could be beneficial in terms of preventing lipid peroxidation in meat [146, 147, 160] but more importantly, selenium is absolutely essential

for expression of GI-GSH-Px, the main defense against lipid peroxide absorption in GIT [36]. Selenium is also important for expression of other selenoproteins (e.g., thioredoxin reductase etc.), which play an important role in antioxidant defense in the intestine and in other tissues. In fact, Se-enriched eggs, meat, and milk are already on the market in various countries in the world [30, 31].

- To improve product storage by decreasing oxygen availability and lipid peroxidation. To minimize storage of cooked products, which are especially susceptible to peroxidation
- In the fast-food restaurants, to change frying oils more often and use olive oil which is less sensitive to peroxidation [161] and to enrich frying oils with natural antioxidants (e.g., tocopherol mixture). It would be an advantage to serve fast food with bigger portions of salads and use more sauces providing additional antioxidants. Some other oils (e.g., rapeseed oil) enriched with tocopherols can also be considered to be useful.
- To produce antioxidant-enriched sources, especially for fast-food restaurants.

Therefore, it is possible to provide consumers with a range of animal-derived products with nutritionally modified composition in such a way that they can deliver substantial amount of health-promoting nutrients to improve the general diet and help to maintain good health, in fact, in the United Kingdom in main supermarkets there are such products (Tesco, Morrisons, etc.). Therefore, without changing habits and traditions of various populations it is possible to solve problems related to deficiency of various nutrients, in particular selenium. The consumer will go to the same supermarket to buy the same animal-derived products (egg, milk, and meat), cook and consume them as usual. The only difference will be in the amount of specific nutrients delivered with such products.

7.2 At the Consumer Level

- To choose olive oil for frying food. This will decrease accumulation of oxidation products [161] and will be beneficial in terms of decreasing omega-6 PUFA consumption and increasing MUFA consumption in accordance with recent health-related findings [162]. Rapeseed oil enriched with tocopherols is also an important choice.
- To use more spices and herbs during cooking. This will decrease oxidation and prevent accumulation of the lipid peroxides.
- To decrease usage of cooked meals after storage.
- To decrease consumption of fast food, prepared by current technology of deep-frying. Use more sauces, which can provide additional antioxidants.
- To make sure that meat meals are served with plenty of vegetables, providing necessary antioxidants.
- To increase vegetable and fruit consumption on everyday basis.

Therefore, since we cannot avoid prooxidants in our food we need to make sure that they are compensated by consumption of increased levels of natural antioxidants. For this reason, it would be advantage if our meat and fish meals are served with plenty of vegetables. Various sauces (e.g., tomato sauce) could provide additional antioxidants. Red wine could also add additional flavonoids as a source of antioxidants. Various juices are also good sources of natural antioxidants

as well as fruits. If a meal is finished with tea, this will also add to antioxidant potential of the digesta.

All these suggestions are in the line of traditional meals served in various countries of the world. Antioxidants compensate prooxidants and a positive balance in the digestive tract is the first step to healthy life.

All the future exists in the past.

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