PREFACE

This book presents an overview of lipid peroxidation: inhibition, effects and mechanisms. The topics analyzed, cover a broad spectrum of functions played by lipid peroxidation and presents new information in this area of research. The topics analyzed include: progress in the knowledge of lipid peroxidation, from the first evidences issued by Nicolas Theodore de Saussure in Paris 1804; fighting against lipid peroxidation: the unique story of docosahexaenoic acid in the brain; protective effects of melatonin and structurally-related molecules in reducing membrane rigidity due to lipid peroxidation; synergistic effects of antioxidant compositions during inhibited lipid autoxidation; lipid peroxidation and animal longevity; free radicals in health and disease; lipid peroxidation in autoimmune diseases; aldehydes derived from lipid peroxidation in cancer and autoimmunity; the role of reactive oxygen species and lipid peroxidation in the neurodegenerative process after spinal cord injury; kinetics and mechanisms of inhibited lipid autoxidation in presence of 4-substituted-coumarins; hypoxia and oxidative stress: cell signaling mechanisms and protective role of vitamin C and cilnidipine; characterization of oxidative stress and antioxidant potency; paying attention to time and location; lipid peroxidation in aquatic organisms: ontogenetic, phylogenetic and ecological aspects; chemistry of lipid oxidation in edible oils; and menopause progression and oxidative stress: associated mechanisms and the importance of physical exercise.

Chapter 1 - The first evidences for the peroxidation of lipids were published in Paris 1804 by the Swiss chemist Nicolas–Theodore de Saussure in the book "Recherches chimiques sur la végétation" In his book he described the principal components of plants, their synthesis and decomposition. New observations on the chemical performance of plant lipids lay the basis of the understanding of their oxidative properties. The major credit for developing the hydroperoxide hypothesis of lipid autoxidation is due to Farmer and co-workers, reported in the 1940s (Farmer et al., 1943). Later in the 1950s, the significance of lipid peroxidation to biological systems and medicine began to be widely explored. In this chapter, the author reviews the progress in the knowledge of lipid peroxidation, from the first evidences issued by Nicolas - Theodore de Saussure and then the author describes important hand marks in the knowledge of lipid peroxidation from 1940s up to now. The author also reviews some basic concepts of the chemistry and biochemistry of lipid peroxidation as well as specific markers of lipid peroxidation.

Chapter 2 - Brain parenchyma is extremely sensitive to oxidative stress. Several factors determine such susceptibility. First, brain is highly enriched in polyunsaturated fatty acids,

which are easily peroxidable. Second, brain tissues contain high contents of transition metals, such as iron and copper, which favour the so-called Fenton reactions. And third, the high rate of aerobic metabolism of nerve cells yields reactive oxygen species (ROS) as a consequence of incomplete metabolic reduction of oxygen to water. Paradoxically, brain is the organ containing the largest amount of docosahexaenoic acid (DHA) in the whole body, which, in turn, is predominant amongst all fatty acids in the brain membranes. The question arises on how this highly peroxidable polyunsaturated fatty acid can be homeostatically regulated to be protected from oxidative stress in nerve cell membranes. Recent evidences have aid to unravel part of the mechanisms whereby DHA levels are preserved in such pro-oxidant scenario, without substantial peroxidation. Indeed, beyond its essential role as membrane phospholipid constituent, DHA is also a powerful modulator of transcriptional activity in nerve cells. Thus, DHA can efficiently stimulate gene expression of different antioxidant complexes, including thioredoxin and glutathione systems. Noteworthy, DHA is a powerful modulator of different isoforms of the phospholipid-hydroperoxide glutathione peroxidase (*Gpx4*) gene expression. GPx4 is unique in that it is the only family of isoforms capable of reducing oxidized phospholipids in membranes without the need of deacylation by phospholipase A2 (PLA_2). The final scenario is that DHA modulates neuronal antioxidant capacity to ensure its self-protection from oxidative threats.

Chapter 3 - Lipid peroxidation is the expression of free radicals damage in biological membranes. The biochemical reaction is an autooxidative and degenerative process in which the acyl chains of the phospholipids are especially vulnerable to free radical attack. Structural changes in biomembranes produced during lipid peroxidation disrupt molecular motion in the membrane and tends to increase phospholipid bilayer rigidity. Changes in membrane fluidity are critically important for the homeostasis of numerous cell functions. Even slight changes in membrane fluidity may cause aberrant cellular function and induce pathological processes. Thus, there is considerable interest in molecules which are able to preserve fluidity levels in the membranes because of their protective effects against lipid peroxidation.

The discovery of melatonin as a highly efficient free radical scavenger and general antioxidant in a wide variety of tissue homogenates and organisms as well, has stimulated a large number of studies related to the ability of this molecule to stabilize membranes from oxidative damage. While numerous reports have shown the ability of this indoleamine to preserve optimal levels of fluidity in biological membranes and to resist the rigidity induced by free radical attack, there is little information regarding the antioxidant ability of other indoleamines and β-carbolines synthesized in the pineal gland. In the present work, the authors review the current findings related to the beneficial effects of melatonin and structurally-related compounds in maintaining the fluidity of biological membranes against lipid peroxidation, and further, the authors discuss its implications in ageing and disease.

Chapter 4 - Biologically active compounds with antioxidant potential, i.e., bio-antioxidants (natural and their synthetic analogs) have a wide range of applications. They are important drugs, antibiotics, agrochemical substitutes, food preservatives, etc. Many of the drugs today are synthetic modifications of naturally obtained substances with both biological and antioxidant activities. Nowadays bio-antioxidants play an important role in disease prevention as components of food additives and antioxidant drugs in mono- or in complex therapy.

Twenty antioxidant compositions, containing mono-, bi- and polyphenols, have been selected for this study. Various kinetic parameters and theoretical descriptors were applied to

explain the effects observed and mechanisms of action of these antioxidant compositions. It has been proven that the synergism observed between components in the studied mixtures is mainly due to regeneration of the stronger antioxidant in the binary mixture.

If two or more antioxidants are added to the oxidizing lipid substrate, their combined inhibitory effect can be additive (summary), antagonistic (negative) or synergistic (positive). Different effects of various antioxidant compositions were compared and discussed. Synergism - when the combined inhibiting effect of the mixture ($IP_{AOH + TOH}$) is higher than the sum of inhibiting effects ($IP_{AOH} + IP_{TOH}$) of the individual components, i.e., $IP_{AOH + TOH} > IP_{AOH} + IP_{TOH}$. Additivism - when the antioxidant mixture ensured the same inhibiting effect as the sum of the inhibiting effects of the individual components, i.e., $IP_{AOH + TOH} = IP_{AOH} + IP_{TOH}$. Antagonism - when the combined inhibiting effects of the antioxidant mixtures is lower/weaker than the sum of the individual components, i.e., $IP_{AOH + TOH} < IP_{AOH} + IP_{TOH}$.

The synergism observed can be explained by two kinds of reaction mechanisms:

- H atom transfer from the studied antioxidant (AOH) to the tocopheryl radical ($TO^{\bullet}$), which is reversible, but in case of synergism the equilibrium is shift to the right direction, i.e., to the regeneration of TOH, which is the stronger antioxidant.
- Cross-dissproportionation reaction between phenoxyl ($AO^{\bullet}$) and tocopheryl ($TO^{\bullet}$) radicals with regeneration the stronger antioxidant (TOH) and formation of quinone (A = O) from AOH.

In case of antagonism between AOH and TOH:

- H atom transfer leads to the regeneration of the weaker antioxidant (AOH), but not the stronger one (TOH).
- Cross-recombination reaction between both phenoxyl radicals ($AO^{\bullet}$) and ($TO^{\bullet}$) to inactive compounds is preferred.
- Cross-dissproportionation reaction between both phenoxyl radicals ($AO^{\bullet}$) and ($TO^{\bullet}$) with the regeneration of the weaker antioxidant (AOH) and tocopheryl methylene quinone (T = O) formation.

The behavior of the studied antioxidants (AOH) when mixed with TOH has been rationalized on the basis of the calculated BDEs (Bond Dissociation Enthalpies), chemical structures of the molecules and the possible formation of intermolecular complexes. New equations for determination of different effects observed (synergism and antagonism) and calculation (in %) are proposed here for the first time.

Chapter 5 - Ageing is universal among animals and different animal species have distinctive maximum lifespans. This variation in longevity achieved by evolution is several orders-of-magnitude greater than that achieved by experimental or genetic manipulation and can provide considerable insight into the mechanisms of ageing. Following the observation that membrane fatty acid composition varies with body size among mammal species, it became apparent that the fatty acid composition of membrane lipids was also strongly correlated with the maximum lifespan of mammals. This emphasised the importance of lipid peroxidation in ageing and determination of longevity. While saturated and monounsaturated fatty acids are resistant to lipid peroxidation, polyunsaturated fatty acids are peroxidised and the more polyunsaturated the fatty acid the more susceptible it is to peroxidation. It is possible to calculate a peroxidation index (PI) for a particular membrane fatty acid composition and this PI value expresses the calculated susceptibility of the membrane to peroxidative damage

as well as the relative abundance of secondary lipid-based reactive species produced by the primary ROS made from mitochondrial respiration. The PI value of membranes is inversely related to lifespan of mammals. Furthermore, exceptionally long-living mammal species (naked mole rats, echidnas and humans) have membrane lipid PI values lower-than-expected for their body size but as expected for their specific lifespan. Similarly, within a mammal species (mice) long-living strains have membrane lipids with a low PI. The experimental treatment of calorie-restriction, known to extend lifespan of mammals, has also been shown to decrease membrane PI values. Birds are longer-living than similar-sized mammals and show the same relationship between membrane composition and longevity. An inverse relationship between membrane lipid PI and longevity is also observed in invertebrates, although it is not the same precise relationship as observed in mammals and birds. Experiments to test the link between maximum longevity and membrane composition via diet manipulation have been generally unsuccessful because membrane PI appears to be homeostatically regulated with respect to diet PI. Other recent experimental alterations of membrane composition (e.g., by RNA*i* knock-down in *C. elegans*) support a link between membrane fatty acid composition, resistance to oxidative stress and longevity. Other aspects of membrane lipid composition (e.g., plasmalogens and non-methylene-interrupted fatty acids) may also be important for some species. These observations suggest lipid peroxidation is central to the biology of ageing and the determination of the distinctive longevities of different animals.

Chapter 6 - Free radicals and consequent lipid peroxidation process and lipid peroxides have direct effects on cell growth and development, cell survival and play a significant role in various diseases including cancer. During the electron-transport steps of ATP production, due to the leakage of electrons from mitochondria, reactive oxygen species (ROS), e.g., superoxide anion (O_2-.) and hydroxyl (OH.) radicals, are generated. These ROS, in turn, lead to the production of hydrogen peroxide (H_2O_2), from which further hydroxyl radicals are generated in a reaction that depends on the presence of Fe^{2+} ions. Free radicals and lipid peroxides have both beneficial and harmful actions. Free radicals are needed for signal-transduction pathways that regulate cell growth, reduction-oxidation (redox) status, and as a first line of defense by leukocytes against infections. Paradoxically, excess of free radicals and lipid peroxides start lethal chain reactions that can inactivate vital enzymes, proteins and other important subcellular elements needed for cell survival and may also induce apoptosis. Thus, free radicals and lipid peroxides are like a double-edged sword and play a significant role in health and disease. Physiological amounts of free radicals and lipid peroxides are needed for normal health of cells, tissues and organs while excess may induce sufficient damage to cells and tissues and lead to their dysfunction and disease(s). In view of their potent actions, concentrations of free radicals and lipid peroxides are regulated by the antioxidant status of cells. Thus, the balance between free radicals and lipid peroxides and antioxidants is important for normal health and disease. There is evidence to believe that free radicals, lipid peroxides and antioxidants participate in inflammation, immune response and thus, play a significant role in atherosclerosis, cardiovascular diseases, Alzheimer's disease, cerebrovascular diseases, Parkinson's disease, and other neurodegenerative and/or neuroinflammatory diseases, rheumatological conditions, obesity, diabetes mellitus, hypertension, metabolic syndrome, cancer and several other diseases/disorders. Hence, methods designed to fine tune free radicals/lipid peroxidation/antioxidant status of cells may form a new approach to several diseases.

Chapter 7 - Auto immune diseases (AIDs) comprise over 80 different disorders that affect 1-2% of the world population. AIDs are triggered by genetic, environmental and metabolic factors affecting mucous, gastric, cutaneous, neuronal, connective, lung, bone and other tissues. The reported low antioxidant levels in autoimmune diseases suggest a redox imbalance and evidence that oxidative stress and oxidative modifications to biomolecules generating neoepitopes triggering an exacerbated inflammatory response and a major role in pathophysiology of these diseases. Increased carbonyl content and lipid hydroperoxides quantified in biological fluids evidences for an active role of lipid peroxidation in the onset and progression of autoimmune diseases. Lipid peroxidation is a very complex chain reaction that generates an overwhelming array of lipid peroxidation products (LPP) with epitopes recognized by the immune system and able to modulate the immune response. Given the complexity of the LPP likely to be formed, their accurate identification and quantification in the various biological fluids is challenging.

This chapter describes the current knowledge on LPP identified in AIDs, their levels in fluids, cells and tissues, and methodological approaches applied for their detection and quantification. An overview on the advantages and limitations associated with the identification and quantification using specific and unspecific strategies will also be provided. Based on the findings, the authors describe their role in the onset and resolution of immune response and the validity of lipid peroxidation products (LPP) as potential AIDs biomarkers for early diagnosis and monitoring disease status.

Chapter 8 - The unsaturated aldehydes derived from lipid peroxidation (LPO), such as 4-hydroxy-2-nonenal (HNE), which are characterized by high chemical reactivity, diffusibility, and relatively long life, are considered to act as second messengers of oxidative stress. The majority of the cellular effects of reactive aldehydes are mediated by their interactions with either low-molecular-weight compounds, such as glutathione, or macromolecules, as proteins and DNA. In particular, aldehyde-protein adducts have been extensively investigated in disease conditions characterized by the pathogenic contribution of oxidative stress, such as cancer and autoimmune diseases.

In cancer, these aldehydes can act as either positive or negative regulators, depending on their concentration and the tissue considered. As a consequence, the role of reactive aldehydes in cancer is double-sided. The 'dark-side' of reactive aldehydes has to do with their carcinogenic potential, while they also display anti-cancer effects, such as the inhibition of cell proliferation, angiogenesis, cell adhesion and the induction of differentiation and/or apoptosis in various tumor cell lines.

The modification of self antigens via the formation of adducts of unsaturated aldehydes, such as HNE, is also linked to the breaking of immunological tolerance to self antigens in various autoimmune diseases. In experimental mice, T cell sensitization to HNE-modified autoantigens, such as SS-A2/Ro60, a prominent autoantigenic target of antinuclear autoantibodies in systemic lupus erythematosus (SLE) and Sjögren syndrome (SS), promoted the intramolecular spreading of the immune response to formerly tolerated epitopes of the native self antigen and the intermolecular spreading to other protein antigens and to DNA. Further investigations of the molecular mimicry between the adducts of HNE and its analog 4-oxo-2-nonenal (ONE) with proteins and DNA and of the specificity of antibodies found in mice immunized with HNE-modified proteins and in patients with SLE suggest that HNE-containing neoepitopes formed upon HNE generation and reaction with cell proteins can be instrumental for the breaking of immunological tolerance to self protein antigens and for the

production of bispecific autoantibodies, cross-reacting with native and aldehyde-modified DNA.

Chapter 9 - The discovery of free radicals in biological materials first took place 50 years ago. Free radicals are classified as reactive nitrogen species (RNS) or reactive oxygen species (ROS). The latter are known to be responsible for the oxidation of lipids, proteins and DNA. Ordinarily, antioxidants ensure the maintenance of the appropriate redox homeostasis. The problem occurs when these protective mechanisms are overtaken by the excessive presence of ROS. Therefore, the presence of the latter results in significant functional consequences in a variety of diseases.

The central nervous system (CNS) is an easy target for ROS due to its low antioxidant level and high concentration of Fe^{2+}, oxygen, and polyunsaturated fatty acids (PUFAs). Consequently, the activation of auto-destructive mechanisms after spinal cord injury (SCI), such as the inflammatory response, induce an elevated presence of ROS and lipid peroxidation (LP) of PUFAs, which lead to axonal demyelination and cell death. LP is perhaps one of the most important tissue damaging phenomenon after SCI. LP is a process that spreads over the surface of the cell membrane altering the PUFAs, which in turn causes an impairment of phospholipid-dependent enzymes, disruption of ionic gradients, and even membrane lysis. These alterations reduce the generation and transmission of electrical potentials, and causes membrane and motor dysfunction. A significant increase in LP products is observed after SCI as early as 15 min after injury. Two well-characterized and highly toxic products of LP in SCI are 4-hyroxynonenal (4-HNE) and acrolein.

LP after SCI is caused by elevated free radical concentrations that are released primarily by inflammatory cells. In fact, evidence shows that the presence of infiltrating inflammatory cells is significantly correlated with the amount of tissue damage after injury. When the inflammatory response is activated, high concentrations of free radicals, principally superoxide anion (O^{2-}•) and nitric oxide (NO•), are produced. Together, these molecules have the capacity to generate neurotoxic compounds such as peroxynitrite that initiates the LP process.

The discovery of therapeutic strategies that promote neuroprotection has been the aim of several research projects. At the moment, the use of pharmacological compounds is perhaps the most experimentally recurred strategy to counteract LP. These pharmacological interventions include: compounds that either inhibit the formation of ROS and RNS prior to the initiation of LP, compounds that inhibit the propagation of LP reactions or the use of scavengers for lipid radicals (LOO•) and the alkoxyl radical (LO•) posterior to the initiation of LP.

Protective autoimmunity is an innovative strategy based on the modulation of autoreactive mechanisms in order to promote neuroprotection. Evidence has demonstrated that immunization with neural-derived antigens modulates this autoreactive response and inhibits LP after SCI. Several neuroprotective strategies have been proposed, in order to decrease the amount of ROS, NO• and LP after SCI. The first objective of this chapter is to describe the relationship between ROS, lipid peroxidation, and the inflammatory response after SCI. The second objective of this chapter is to describe the effects of diverse therapeutic strategies in the before-mentioned mechanisms.

Chapter 10 - Coumarins are a large group of 1,2-benzopyrones derivatives widely distributed in natural plant sources. They have been studied *in vivo* and *in vitro* for their biological activities: anti-inflammatory, anti-carcinogenic, anti-viral, anti-thrombotic, anti-

allergic, hypo-lipidemic and antioxidant activity. Some of them are considered to be interesting compounds for pharmaceutical research because of their wide spectrum of potentially positive pharmaceutical activities. Especially their antioxidant, anti-aggregant, lipid lowering, anti-inflammatory and vasorelaxing effects may predetermine them for the treatment and/or prevention of cardiovascular diseases. In fact, rare *in vivo* studies on coumarins suggested their positive role in the treatment of some cardiovascular diseases. However, the biochemical mechanisms underlying these effects are not clear. Some of the pharmaceutical activities of coumarins could be ascribed to their capacity to inhibit lipoxygenase and cycloxygenase and to scavenge reactive oxygen species.

The antioxidant activity, as well as biological activity, of these compounds is strongly influenced by their chemical structure. The tendency to form mutagenic and toxic 3,4-coumarin epoxide intermediates during metabolic degradation of 3,4-unsubstituted coumarins has limited their pharmaceutical application. Design of novel derivatives of coumarins (as drugs) may be a good strategy to overcome this problem. In contrast to unsubstituted coumarins, 4-substituted ones do not induce formation of epoxide. For this reason, they could be better candidates for pharmaceutical use. For example, 4-methylcoumarins are known to have some pharmaceutical *effects:* choloretic, analgetic, anti-spermatogenic, anti-tubercular, anti-diuretic, anti-inflammatory activities. 4-Hydroxycoumarins have a lot of applications as drugs with anticoagulant, spasmolytic, bacteriostatic, potential anti-HIV, antifungal and herbicide activities. Some of them are known for their antibiotic activity; furthermore some of them show low toxicity and dose-dependent anticoagulant activity *in vivo*. The most widely used antithrombotic agent in USA and Canada is racemic sodium Warfarin. All compounds of this group inhibit Vitamin K epoxide reductase, however, they cause some side effects. By synthesis of different 3,3'-arylidene-bis-(4-hydroxy-2H-chromen-2-ones) it is possible to obtain compounds with biological activity comparable to that of Warfarin, but with low toxicity and lower side effects.

The study of the antioxidant inhibiting activity is an exciting challenge from both experimental and theoretical viewpoints. A comprehensive knowledge of the chemical and functional properties and antioxidant activities of 4-methyl-, and 4-hydroxycoumarin derivatives could help to develop design strategies for creating non-toxic coumarins with antioxidant activity. Here the authors present the structure-antioxidant activity relationships of over forty 4-substituted coumarin derivatives (mainly 4-methyl-, and 4-hydroxycoumarins) studied by using combined experimental and theoretical approaches: radical scavenging activity, chain-breaking antioxidant activity during inhibited lipid autoxidation and theoretical methods using the density functional theory (DFT) for the calculation of quantum chemical features. The fundamental role of catecholic moiety in the inhibiting activity and the importance of substituents at positions 3 and 4 for the molecular structure are discussed.

Chapter 11 - Hypoxia is a pathological condition that can directly impair the metabolic pathways in the living cells. Interestingly, physiological hypoxia is an important micro-environmental signal, in a range of processes including new blood vessel formation (angiogenesis) during development, wound healing, regulation of vascular tone and response to exercise. Its effects are usually mediated via the activation of hypoxia inducible factor 1 (HIF-1α), besides nitric oxide (NO) - an important key factor of hypoxia-induced responses. The low oxygen sensing at the cellular level exerts its defense through HIF-1α by increasing hypoxia adaptability but it cannot prevent the generation of free radicals through endothelial cellular oxidative stress which may lead to lysosomal, mitochondrial and microsomal

damage, resulting in organelle dysfunction. Beside these actions, hypoxia induced oxidative stress greatly impairs cell signal transduction by altering gene expression in hypoxia sensitive tissues. It has also been found that cellular adaptation to low oxygen is compromised in the presence of hyperglycemia, culminating in increased cell death and tissue dysfunction. An excessive accumulation of reactive oxygen species can elevate antioxidant enzymes and then impair beta cell functions. Recent observation reveals that chronic intermittent hypoxia (CIH) activates NADPH oxidase which is very important for HIF-1α expression and ROS production. NADPH oxidase hyperactivity also changes intracellular calcium homeostasis and stimulate further HIF-1α production, subsequently resulting in more ROS generation. High concentration of ROS excites carotid bodies that influences sympathetic adrenergic activities via chemoreflex, alters catecholamine and insulin secretary mechanisms.

A link between hypoxia and glucose homeostasis has already been established. Present authors further ascertained that glucose homeostasis due to hypoxia can be modulated by supplementation of either vitamin C or L/N type calcium channel blocker, cilnidipine.

This chapter provides understanding of the relationship between hypoxia induced increased sympathetic activation and consequent impaired glucose homeostasis. The chapter also highlights how hyperglycemia augments oxidative stress and induces the overproduction of ROS which modulates HIF-1α regulation and possible protective actions of antioxidant (vitamin c) and L/N type of Ca^{++} channel blocker (cilnidipine) against hypoxia induced altered pathophysiology in mammalian systems.

Chapter 12 - Most of the commonly used assays of oxidative stress (OS) are based on the level of the studied biomarker, as measured at one time-point. OS, as evaluated with different assays do not correlate with each other, so that OS cannot be defined in universal terms. Furthermore, some biomarkers are not very stable in withdrawn blood and their level may depend on whether their level is measured immediately after being withdrawn or a half an hour later, particularly if the assay involves a stage of pretreatment. Most assays of antioxidants are conducted in solutions, whereas in biological systems amphiphilic phospholipids reside either in membranes or in emulsion micro-emulsion particles (lipoproteins) and peroxidation therefore occurs at the lipid-water interface. This, in turn, means that the relative activities of different antioxidants should be assayed in the medium of interest. Hence, an assay utilized to compare antioxidants in the search for improved inhibitors of peroxidation used as stabilizers of food-stuff, may have to be considerably different from the assay to be used in the search for antioxidants that will maximize the shelf life of a given drug. The authors propose evaluating oxidative status based on the length of the lag preceding copper-induced peroxidation of serum lipids and ranking antioxidants on the basis of the concentration of antioxidant required to double the lag.

Chapter 13 - Lipid peroxidation (LPO) plays an important role in the evolution of living organisms and their adaptation to various environments. LPO attributes of the organism environmental stress caused the changes of natural conditions and anthropogenic impact. In recent years, there has been considerable interest in the use of biochemical indices within aquatic species, because they are the main source of food for people, and they contain many essential compounds including antioxidants, unsaturated fatty acids, carotenoids, vitamins, and etc. Lipid peroxidation parameters are good biomarkers, characterizing oxidative stress in the aquatic organisms, caused toxicants containing in effluents and sewage. To the other hand, LPO level in the animals depends on their physiological status, stage of development, age, abiotic (seasonal variations, temperature, oxygen concentration, physical and chemical

conditions in the habitats, and etc.), biotic factors (food composition, its consumption, parasitic and microbial infection) and anthropogenic impact. The study of LPO in different species may help to understand the mechanisms of reactive oxygen species (ROS) generation and their role in the origin of life and evolution of the living organisms belonging to various taxa. This chapter discusses the following areas including (1) lipid peroxidation levels in aquatic organisms in their early life and related to age; (2) lipid peroxidation level in the tissues of aquatic animals belonging to different taxa and ecological groups; (3). fluctuations of lipid peroxidation level in aquatic organisms inhabiting locations, characterizing different environmental conditions; (4) use LPO parameters as biomarkers of aquatic animals health, exposed to pollution and toxicants.

Chapter 14 - Edible oils are rich in triacylglycerols, which are made of saturated and unsaturated fatty acids. Triacylglycerols are oxidized by different factors such as light, heat in the presence of oxygen. Triacylglycerols composition plays important role in the chemistry of oxidation process. The formation of triacylglycerol free radicals are the starting point in the free radical mechanism. This chapter provides an insight in to the reaction mechanism of the formation of different primary oxidation compounds of triacylglycerol oxidation. The formation of hydroperoxides of linolenic, linoleic and oleic acids moieties are explained. The mechanism of formation of primary oxidation products such as hydroperoxides, epoxides, hydroxides, epidioxides and epoxy epidioxides are given. The presence of oxidized products of edible plays significant role in the rancidity of foods and health effects in human.

Chapter 15 - The increasing number of elderly people is a phenomenon that encourages the search for strategies to promote health and decrease the risk of age-related diseases. Studies have related that the decrease in physical activity, dyslipidemia, oxidative stress and changes in oxidative enzymes are associated with increased risk of cardiovascular disease in postmenopausal women. Acutely, exercise can increase the production of reactive oxygen species through several mechanisms. Additionally, studies involving chronic responses to exercise suggest that training promotes beneficial adaptations in postmenopausal women. However, studies involving the acute response of oxidative stress markers with different modes of exercise in this population are scarce. Since aerobic and resistance exercise have beneficial effects on the antioxidant system and markers of oxidative stress, the aim of this review is to relate menopause and its progression to oxidative stress and discuss the importance of exercise as a protective factor against oxidative stress.