

**LIPID PEROXIDATION AND ITS ROLE IN THE PATHOGENESIS OF CELL
DAMAGE**

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Abstract: This article discusses the process of lipid peroxidation (LPO) and its role in the pathogenesis of cell damage. Lipid peroxidation is a complex chain reaction that occurs as a result of the oxidation of polyunsaturated fatty acids, one of the main components of biological membranes, under the influence of free radicals. This process leads to negative consequences such as disruption of cell membrane integrity, disruption of ion exchange, mitochondrial dysfunction, formation of cytotoxic aldehydes, and increased oxidative stress. Increased LPO plays an important role in the pathogenesis of cardiovascular diseases, neurodegenerative diseases, atherosclerosis, diabetes, inflammatory processes, and cancer. The article also analyzes the protective mechanisms of the antioxidant system, their function in limiting LPO, and their therapeutic significance.

Keywords: Lipid peroxidation, Free radicals, Oxidative stress, Cell damage, Antioxidants, Membrane dysfunction, Pathogenesis.

Introduction

The normal functioning of cells and tissues in the human body depends on the stability of many complex biochemical processes. One of them is lipid peroxidation (LPO), which is the oxidation of membrane lipids under the influence of free radicals and reactive oxygen species (ROS). Since cell membranes contain a large amount of polyunsaturated fatty acids, they are very sensitive to oxidative processes. Lipid peroxidation can also participate in physiological processes of the body, but its excessive increase leads to serious damage to cell structures, increased oxidative stress and the development of various diseases.

The LPO process is considered one of the leading pathogenic mechanisms in the development of diseases of the cardiovascular system, central nervous system, endocrine system and tumor processes. Therefore, a deep study of lipid peroxidation is important for understanding the pathogenesis of diseases, as well as their prevention and treatment.

Main part

The essence of lipid peroxidation

Lipid peroxidation is the process of formation of peroxides (ROOH), hydroperoxides and aldehydes as a result of the reaction of polyunsaturated fatty acids with free radicals. The process consists of three stages:

1. Initiation (beginning) – RCT or metal ions (Fe^{2+} , Cu^{2+}) form a lipid radical by removing a hydrogen atom from fatty acids.

2. Propagation (chain reactions) – lipid radicals combine with oxygen to form lipid peroxide radicals. These radicals attack another lipid molecule, forming new radicals.

3. Termination (end) – the process is stopped by reacting with antioxidants or other radicals.

Lipid peroxidation has a chain and accelerating nature, and one molecule of RCT can oxidize thousands of lipid molecules.

Main products of lipid peroxidation

- Malondialdehyde (MDA) – one of the most important markers of LPO, reacts with DNA and proteins and has a toxic effect.
- 4-hydroxynonenal (4-HNE) – leads to denaturation of membrane proteins, decreased enzyme activity, and disruption of cell signaling.
- Lipid hydroperoxides – weaken the mechanical strength of the membrane.

These substances are cytotoxic and trigger irreversible processes inside the cell.

Effect of lipid peroxidation on the cell membrane

The LPO process significantly changes the cell membrane structurally and functionally:

- Integrity disruption – the membrane becomes fragile, “holes” appear.
- Increased permeability – the irregular entry and exit of Na^+ , Ca^{2+} , Cl^- ions disrupts the balance inside the cell.
- Failure of ion pumps – especially the activity of Na/K-ATPase and Ca-ATPase decreases.
- Weakening of the mitochondrial membrane – ATP synthesis decreases, apoptosis pathways are activated.
- Decreased receptor functions – cell signals are incorrectly perceived.

All this poses a threat to the normal survival of the cell.

The role of lipid peroxidation in the pathogenesis of cell damage

Development of oxidative stress

Oxidative stress occurs when the amount of antioxidants (SOD, catalase, glutathione peroxidase, vitamins E and C) in the body decreases or RKT increases. This leads to the persistence of LPO at a high level.

Activation of apoptosis and necrosis

4-HNE and MDA cause an increase in mitochondrial permeability, which leads to:

- release of cytochrome C,
- activation of caspases,
- initiation of apoptosis.

In severe damage, the cell undergoes necrosis.

Biochemistry of atherosclerosis

LP is a central link in the pathogenesis of atherosclerosis. LDL lipoproteins circulating in the blood are oxidized by free radicals and converted to oxidized LDL (oxLDL). OxLDL is biochemically characterized by:

- carbonylation of its proteins,
- hydroperoxidation of the lipid core,
- oxygenation of its surface phospholipids

These changes increase their recognition and phagocytosis by macrophages, leading to the formation of foam cells. Foam cells are the primary substrate of atherosclerotic plaques. As a result of this process, the endothelium is damaged, nitric oxide is reduced, and inflammatory mediators are increased - all of these are direct biochemical consequences of LP.

The role of LP in the biochemistry of diabetes

In diabetes, increased glucose increases the production of ROS. This increases oxidative stress through glycosylated proteins. As a result of LP:

- MDA,
- 4-hydroxynonenal (4-HNE),
- lipid hydroperoxides

are sharply increased.

The biochemical effects of these substances:

- thicken the basement membrane of blood vessels,
- oxidize collagen and elastin,
- inactivate endothelial NO-synthase.

As a result, diabetic retinopathy, nephropathy and angiopathies are formed.

Intensification of the inflammatory process

The products formed as a result of lipid peroxidation activate transcription factors such as NF- κ B, increasing the production of inflammatory mediators.

Brain cells contain a large amount of phospholipids and have high oxygen consumption, but relatively low antioxidant defense. Therefore, neurons are very sensitive to LP.

Biochemical mechanisms:

- 4-HNE modifies the protein tau and beta-amyloid, enhancing their aggregation.
- MDA covalently binds to DNA and causes mutations.

- As a result of LP, membrane ion channels are disrupted, calcium homeostasis is disrupted.

These mechanisms are one of the molecular bases of Alzheimer's, Parkinson's, and Huntington's diseases.

The role of lipid peroxidation in the pathogenesis of diseases

1. Cardiovascular diseases

Oxidized LDL plays an important role in the development of atherosclerosis. Oxidized lipids form endothelial damage and atheroma plaques.

2. Neurodegenerative diseases

Nervous tissue is very sensitive to LPO because it is rich in fats.

4-HNE is found in high amounts in diseases such as Alzheimer's, Parkinson's, and ALS.

3. Diabetes

Hyperglycemia increases the formation of RCTs and activates the LPO process. This is a major factor in vascular, kidney, and nerve damage.

4. Cancer

LPO products can damage DNA, increase mutations, and form tumor cells.

5. Inflammatory diseases

In diseases such as arthritis, hepatitis, and enterocolitis, LPO contributes to the duration and severity of inflammation.

The body's antioxidant defense system

The body fights lipid peroxidation through:

- Enzymatic antioxidants:

- o superoxide dismutase (SOD),

- o catalase,

- o glutathione peroxidase.

- Non-enzymatic antioxidants:

- o vitamin E,

- o vitamin C,

- o beta-carotene,

- o coenzyme Q10,

- o flavonoids.

This defense system neutralizes radicals and stops the LPO chain reactions.

Conclusion

Lipid peroxidation is an integral part of cellular metabolism, which occurs in small amounts under normal conditions and is controlled by the body's antioxidant system. However, under conditions of oxidative stress, an increase in LPO poses a serious threat to cells, especially membranes and mitochondria. This process plays a central role in cell damage, inflammation, apoptosis, and the pathogenesis of many chronic diseases. Therefore, a deep study of the mechanisms of lipid peroxidation, as well as the improvement of antioxidant-related prevention and treatment methods, is one of the important tasks of modern medicine.

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