Lipid peroxidation

Lipid peroxidation (lipoperoxidation) is **oxidative damage to higher fatty acids**. Lipoperoxidation can occur due to the action of **free radicals** (substances with sufficient affinity for electrons). These substances are capable of ``tearing out a hydrogen atom *(proton and electron) from the methylene group of MK. The abstraction of a proton can start a chain reaction where the damaged molecule acts as a free radical on a neighboring molecule.*

Lipoperoxidation is most often involved in the "hydroxyl radical •OH", the "alkyl radical RO•" and the "peroxyl radical ROO•".

Peroxidation is mainly caused by "unsaturated higher fatty acids", which are part of phospholipids biological membranes and plasma lipoproteins. Fatty acids that contain two or more double bonds separated by a methylene group (linoleic acid, linolenic acid, arachidonic acid) are the most susceptible to it. Saturated MK are subject to peroxidation only exceptionally.

Course of lipid peroxidation

Initiation

Peroxidation of fatty acids

A hydrogen atom is split off from MK by the action of a free radical. This creates a **fatty acid free radical (L•)'** and water.

$L–H + HO• \rightarrow H_2O + L•$

Removal of hydrogen causes a rearrangement. In the original fatty acid, two double bonds were separated by two single bonds. After the rearrangement, the two double bonds are separated by only one single bond and a *conjugated diene* (very reactive) is formed.

The conjugated diene reacts with the oxygen present to form a ``peroxyl radical (L–O–O•).

$L• + O_2 \rightarrow L–O–O•$

Promotion

The peroxyl radical is a very reactive compound. It takes a hydrogen atom from a neighboring fatty acid and transforms into **lipoperoxide (LOOH)*. The fatty acid becomes a radical that can attack other molecules - a chain reaction***.

$L–O–O• + L–H \rightarrow L• + L–O–O–H$

We refer to lipoperoxides as '*primary products* of lipid peroxidation.

The further fate of primary products leads to the formation of **secondary products*. These can be formed by ``cyclization* without changing the number of carbon atoms, by ``fission *to form aldehydes, hydrocarbons or oxoacids with a lower number of carbons, or by ``polymerization*.** We are able to detect compounds formed in this way (e.g. malondialdehyde – toxic, binding to proteins – changing their function) in the laboratory.

Termination

The chain reaction can be terminated:

- when the substrate is exhausted,
- mutual reaction of two radicals,

  $L• + L• \rightarrow L–L$
  $L• + L–O–O• \rightarrow L–O–O–L$
  $L–O–O• + L–O–O• \rightarrow L–O–O–L + O_2$

- by the action of antioxidants (tocopherol).

  $L–O–O• + T–OH \rightarrow L–O–O–H + T–O•$ (not reactive enough)

Consequences of lipoperoxidation

Due to the action of free radicals, there is a change in the structures and biological functions of the attacked compounds. When lipoprotein particles (primarily LDL) are attacked, premature '*atherosclerosis* develops.

Reactive forms not only disrupt the structures of lipids, but also proteins and DNA, leading to their modification, mutations, [[Carcinogenesis|carcinogenesis]], apoptosis, acceleration of the process aging and autoimmune reactions.

Peroxidation of lipids with the participation of transition metals

The course of lipoperoxidation can be accelerated by transition metal ions (iron, copper).

Action of Iron

Iron is an element required for erythropoiesis and the function of some enzymes (respiratory chain, hemoprotein enzymes, cytochromes). It is obtained from food. Absorption depends on its current need. Most of the iron in the body circulates - minimal losses (most often during bleeding).

Free iron practically does not occur in the body. It is usually **bound in enzymes or proteins'** (ferritin, transferrin, lactoferrin). If it occurs freely in the body, it can catalyze the Fenton reaction.

The risk of releasing iron from binding to enzymes and proteins is, for example, during **intravascular hemolysis** (provided that haptoglobin and hemopexin are not sufficient to absorb the released [[Hemoglobin|Hb]]). Furthermore, in **damage to cells containing enzymes** using iron (hepatocytes, heme synthesis). With muscle trauma and release of myoglobin.

Fenton reaction

Fe^{2+} reacts with hydrogen peroxide to form Fe^{3+}, a hydroxide anion and a '*hydroxyl radical* (highly reactive).

$H_2O_2 + Fe^{2+} \rightarrow OH^- + \bullet OH + Fe^{3+}$< /vul>

🔎 *For more information see Fenton reaction.*

Another reaction of free iron in the body

By binding oxygen to hemoglobin, oxyhemoglobin is formed. During this interaction, heme iron Fe^{2+} can be oxidized to Fe^{3+}, where oxygen is converted into **superoxide*. It further affects cellular structures -*** *oxidative stress'*.

The level of reactive forms must be regulated in erythrocytes (and in the whole organism) antioxidant enzymes.

Action of copper

In the blood, copper is bound and transported by **ceruloplasmin'**. Ceruloplasmin with bound copper is responsible for the conversion of Fe^{2+} to Fe^{3+} to avoid the presence of free heme iron and subsequently the Fenton reaction. Copper is necessary for the function of *antioxidant enzymes* (superoxide dismutase), but also of other enzymes such as cytochrome oxidases and tyrosinases.

With a defect in ceruloplasmin (Wilson's disease), there are disturbances in iron transport and thus increased oxidative stress in the body.

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