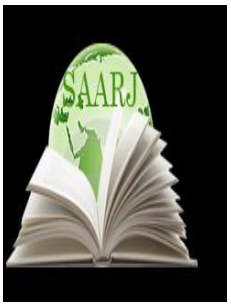

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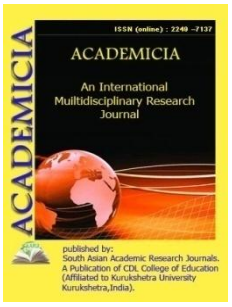

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HOMOCYSTEINE: EFFECT ON BIOCHEMICAL PROCESSES IN THE HUMAN BODY

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ABSTRACT

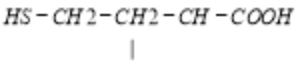
The article presents a review of the literature on the metabolism of the amino acid homocysteine, the emergence of risks for the development of a number of diseases due to excessive accumulation of homocysteine in the human body, and possible ways of correcting hyperhomocysteinemia.

KEYWORDS: *Homocysteine, Homocysteine Metabolism, Hyperhomocysteinemia, Hemocoagulation, DNA Dimethylization, Oxidative Stress, Vitamins Of Group B.*

INTRODUCTION

It is known that modern science is interested in the search for biochemical markers that could reflect the risks of development and the nature of the course of various diseases, as well as predict their outcome ... In recent years, many compounds have been discovered that can reflect and influence the biochemical profile of the body. The metabolic product of methionine, homocysteine, is one of them and attracts the attention of many researchers of various specializations.

Homocysteine. Basic information



Homocysteine ( ) is a sulfur-containing non-protein compound that is synthesized in the body during methionine catabolism. This compound is necessary for the body, but in excess, it can cause oxidative stress, cause genetic mutations, induce cell apoptosis, promote the development of atherosclerosis, regardless of the presence of other atherogenic factors.

Homocysteine Synthesis and Utilization Pathway

Homocysteine is synthesized from methionine in the liver to form SAM, which is a methyl group donor in transmethylation reactions. The optimal concentration of homocysteine in the blood is 5–16 μmol / L and is maintained at this level by two main metabolic pathways: transsulfation with the formation of cysteine or remethylation, ie, the conversion of homocysteine to methionine under the action of the enzyme methionine synthase.

For these reactions to occur, vitamins B6, B12 and folic acid are required (Fig. 1). It is the deficiency of these substances that can lead to hyperhomocysteinemia.

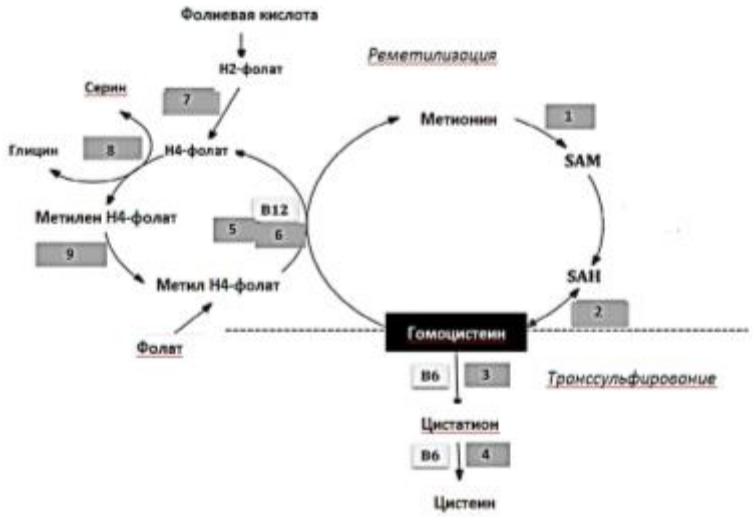


Fig. 1. Simplified scheme of homocysteine metabolism: enzymes: 1 - methionine adenosyltransferase; 2 - s-adenyl-L-homocysteine hydrolase; 3 - cystothion β-synthase; 4 - cystothione γ-lyase; 5 - methionine synthase reductase; 6 - methionine synthase; 7 - dihydrofolate reductase; 8 - serine hydroxymethyltransferase; 9 - methylene tetrahydrofolate reductase

Hyperhomocysteinemia Hyperhomocysteinemia is a condition characterized by elevated levels of homocysteine in the blood.

Causes of hyperhomocysteinemia:

- ❖ hereditary fermentopathies;
- ❖ lack of folic acid and B vitamins in the body;

- gene polymorphism;
- smoking and drinking alcohol;
- hormone-dependent diseases;
- excessive consumption of coffee;
- impaired renal function;
- sedentary lifestyle.

Homocysteine increases the risk of thrombosis, causes DNA methylation and oxidative stress, and damages nerve cells and mitochondria (Fig. 2).

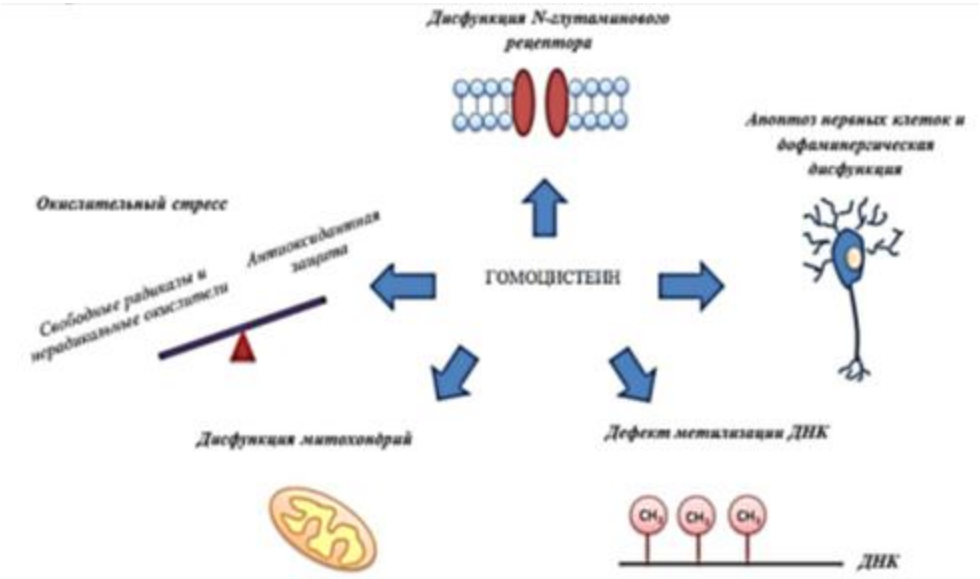


Fig. 2. Mechanism of action of homocysteine

According to the literature, hyperhomocysteinemia can cause resistance of factor V to the action of activated protein C due to the binding of factor V to homocysteine. Homocysteine also blocks the interaction of thrombomodulin with thrombin, which prevents the activation of protein C. Along with this, homocysteine disrupts the binding of antithrombin III with heparan sulfate, which is located on the vascular endothelium, leading to an even greater suppression of the anticoagulant system (Fig. 3)

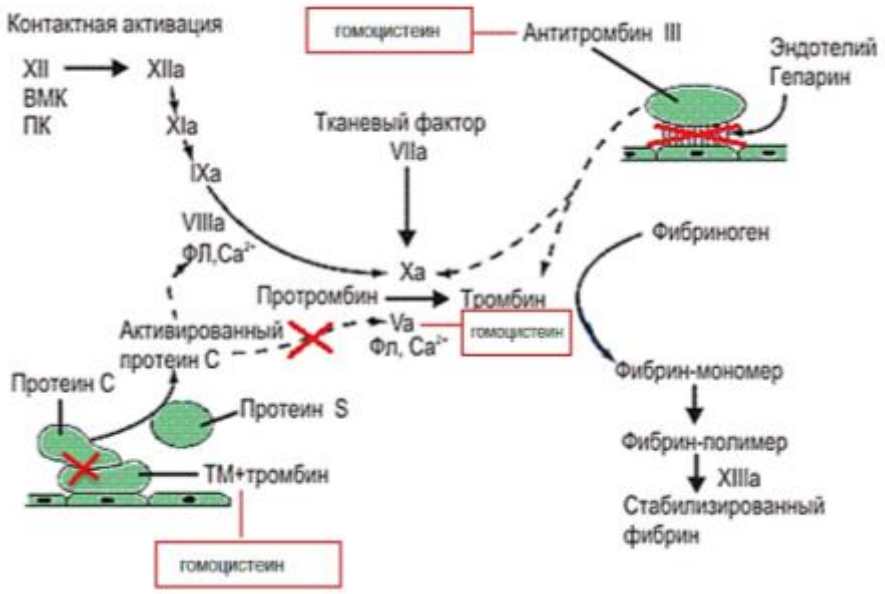


Fig. 3. Influence of homocysteine on the process of hemocoagulation

Normally, annexin II stabilizes the plasminogen receptor S100A10 and facilitates its movement to the cell surface, where the receptor binds to plasminogen and regulates the formation of plasmin. Homocysteine, binding to one of the annexin II domains, blocks the activation of plasminogen, which contributes to the formation of strong blood clots resistant to lysis, as well as an increase in the risk of thrombosis.

Moreover, according to McCullyKS studies, homocysteine damages the endothelium of arteries, initiating the process of activation of cytokines, cyclins and other mediators of inflammation and cell proliferation.

Under the action of homocysteine, reactive oxygen species are formed, which have an oxidative effect on LDL and lipids of endothelial cell membranes, leading to their destruction. An increase in homocysteine concentration can lead to dimethylation of the CpG gene and thus suppress the activity of methyl-CpG-binding protein. As a result, the activity of histone cytylase decreases and the acetylation of histones H3, H4 occurs, which leads to a decrease in gene expression. These processes occur in relation to passive transcriptional chromatin, a change in conformation of which can increase binding by repressor proteins and suppress transcription.

At low glycine concentrations, homocysteine acts as a partial antagonist for the N-glutamate receptor, resulting in hypofunction of glutamatergic transmission, leading to depressive disorders (Fig. 4).

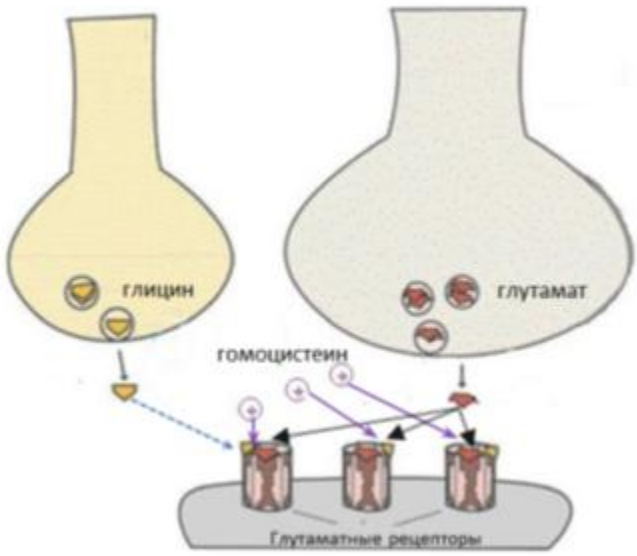


Fig. 4. Interaction of homocysteine with glutamate receptors

Prevention of the damaging action of homocysteine Paraoxonase plays a special role in protecting endothelial cells from the damaging action of homocysteine. This enzyme is localized on HDL and has lactonase activity, which prevents lipoprotein oxidation and detoxifies proteins that have undergone a reaction with homocysteine. B vitamins and folic acid, which are present in sufficient quantities in the body and supplied with food such as greens, cereals, nuts, whole grain bread, the liver participate in the metabolism of homocysteine, catalyzing the reactions of converting it into non-toxic products, and thus prevent the development of hyperhomocysteinemia ...

Prospects for research Already at this stage of the study, the effect of homocysteine on biochemical and pathophysiological processes in the human body is unconditional. It has been proven that hyperhomocysteinemia can indicate disorders in the course of many metabolic pathways and be a risk factor for the occurrence of diseases such as Alzheimer's disease, dementia, myocardial infarction, heart failure, renal failure, atherosclerosis and other diseases associated with vascular damage and tissue ischemia. However, the mechanism of the damaging effect of this compound on mitochondria and on nerve cells is not sufficiently understood, which is an urgent topic for further research.

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