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REGULATION OF MITOCHONDRIAL ACTIVITY BY INCLUSION COMPLEXES OF AMINOPHENOLS AND ANTIMETABOLITES WITH B-CYCLODEXTRINS

X. Chen, A. G. Sysa

*International Sakharov Environmental Institute of Belarusian State University
Minsk, Republic of Belarus
xiandanchen8688@gmail.com*

As a by-product of normal metabolism (endogenous sources) and because of exposure to environmental compounds (exogenous sources), reactive oxygen species (ROS) are formed in all living organisms. Endogenous ROS are largely formed during oxidative phosphorylation in the mitochondria and, therefore, mitochondrial DNA (mtDNA) is at particularly high risk of ROS-induced damage. Mitochondria are essential for cell viability, and oxidative damage to mtDNA has been implicated as a causative factor in a wide variety of degenerative diseases, and in cancer and aging.

Keywords: cyclodextrins, antimetabolites, nanomedicine, polyphenols.

Physiological conditions, oxidative phosphorylation (OXPHOS) produces more than 95% of cellular energy in the form of ATP. This process involves five different protein complexes, complexes 1-5.

OXPHOS directly involves 91 polypeptides, including cytochrome c. These polypeptides are encoded by the nuclear and mitochondrial (mt) genes. Additional proteins are also required for effective OXPHOS, including those for mtDNA stabilization, replication, and transcription; mitochondrial ribosomes; proteins that synthesize heme, flavin, and non-heme iron cofactors, and a variety of proteins involved in the assembly of various complexes.

In general, nearly 300 proteins are required for effective OXPHOS activity. The entire process of oxidative phosphorylation is tightly controlled by the regulation of DNA transcription, RNA translation, substrate feedback inhibition, and the effects of post-translational modifications, including phosphorylation and acetylation, on stability.

Ineffective electron transfer through complexes 1-4 can lead to human disease due to loss of energy metabolism and the generation of toxic ROS following damage to multiple enzymes (especially complexes 1, 2, and 3). Complex V deficiency is also one of the causes of mitochondrial dysfunction.

Compounds containing a purine or pyrimidine ring have a wide spectrum of biological activity: anticancer, antiviral, antiplatelet, analgesic and anti-inflammatory [1-2].

In order to specifically and safely deliver physiologically active substances to target cells, reduce toxicity, increase bioavailability and stability, and prevent degradation, various transport systems are being developed: liposomes, micelles, nanogels, and dendrimers. Cyclodextrins are considered as promising encapsulating polysaccharides. The structure of cyclodextrins, which have an internal hydrophobic cavity, ensures their effective complexation with various drug compounds, which allows the creation of nanoconjugates for the effective delivery of drugs and biologically active compounds to target cells as part of the development of new approaches for the treatment of human diseases ("personalized nanomedicine"). Aminophenols, antimetabolites, and their inclusion complexes with cyclodextrins can act as effector molecules in mitochondrial dysfunction due to their antioxidant and regulatory activity. The relative autonomy of mitochondria, their plasticity and the decisive role in the processes of cellular life activity makes it possible to study a number of metabolic functions and parameters at the level of the cellular subsystem convenient for the researcher, makes it attractive to use mitochondria to elucidate the mechanisms of the purposeful corrective effect of natural substances on metabolically significant processes in the cell.

Despite numerous studies, many patterns and molecular mechanisms of the interaction of polyphenols with cellular components, the structure, physicochemical properties, pharmacological activity of aminophenols and antimetabolites and their complexes with cyclodextrins, the possibility of using complexes to regulate the functional activity of cells, remain unclear.

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