Name of proposed project:

ANTIMUTAGENIC MECHANISMS ACTION OF BIOLOGICALLY ACTIVE SUBSTANCES IN BACTERIAL CELLS IN INDUCED MUTAGENESIS

Author: Gassan Sardarly

E-mail: sardarly@hotmail.com

Related environmental concerns, and in particular, the protection of the gene pool of different species, including human, recently acquired global significance. This is understandable, as a result of human activities in its habitat were and continue to be introduced many thousands of chemical compounds that are mutagenic or potentially mutagenic. For the first time humanity has faced to mutagenic factors and the problem of assessing their effects on the organism in the study of ionizing radiation. Although the basic principles of biological and genetic effects of radiation are clear for a long time, a quantitative assessment and the problem of protection from the effects of radiation hereditary cell structures are not fully studied even today.

In the case of chemical mutagens, complexity of the problem increases many times due to the fact that we are dealing not with one, but with thousands of chemical compounds that differ in their mechanism of action on the cells' DNA chromosomes. Under these conditions, the study of mechanisms of mutagenesis and antimutagenesis for a specific mutagenic factors are futile. The only reasonable way may be the selection of certain types of primary DNA damage induced by mutagens, which behave similarly in the processes of repair and occurrence of mutations. Indeed, now it shows that mutagenesis and repair processes occur qualitatively identically on the broad groups of primary damage. Furthermore, mutations not directly arise from the interaction of photons, or molecules of chemical mutagens with DNA and during the subsequent processes of DNA replication and repair. As a rule, during the flow of these processes, even in the event of DNA damage its original native structure is recovering. Mutations arise from errors in the flow of replication and repair. Moreover, the repair processes (this applies to both the excision and especially for postreplicative repair) have several relatively independent paths, the implementation of which require different enzymes. Only some of these pathways are associated with the induction of mutations, others flow without errors and during the flow of these pathways mutations don't occur. The latter circumstance opens the possibility in principle of stimulation faultless processes of accurate repair, on the other hand, suppression of cellular metabolism units which are involved in the formation of mutations under the influence of mutagens with different nature. Of course, the implementation of this approach requires more in-depth knowledge than we have had so far about the mechanisms of mutation and repair, and comparing such data with the results obtained in the study of the mechanisms of action of specific substances which have antimutagenic activity.

Currently known many compounds having the ability to effectively reduce both induced and spontaneous mutagenesis. These compounds belong to different classes of chemical compounds such as certain amino acids (Slarke, Shankel, 1975), inhibitors of free radical processes (Alekberov et al., 1975), substance intercalating into DNA structure (Clark, 1972), pharmaceutics means (Goncharova , turbines, 1967) and others. These may include some

vitamins, such as C, E, A, K (Shanberger, Rudolph, 1966 Slaga, Bracken, 1977 Sardarly G. M., Guseynov H. I. 1990). The latter is the most promising because of the possibility of their practical use as a prophylactic agent for those who professionally contacts with a variety of hazards (Abutalibov et al., 1978). Despite the relatively large number of publications to identify antimutagens, their mechanism of action remains virtually unexplored. This work is devoted to the analysis of antimutagenic effect of α - tocopherol and other vitamins in E.coli cells, for which genetic and enzymatic control of the mutation process most fully and accurately studied. As a mutagen were used nitroso methyl urea (NMU) and N-methyl-N-nitrosoguanidine (NG), is a typical representative of alkylating mutagens. These compounds induce a wide range of primary DNA damage, mutations of which cause errors due to repair, while other errors during replication. Furthermore, for a greater NG and to a lesser extent NMM characterized selective damage DNA replication fork chromosome along with the stationary direct alkylation of DNA. Furthermore, more for NG and in a less degree for NMM characterized selective damage DNA replication fork of chromosome along with the stationary direct alkylation of DNA. Since the main objective of this work is to determine the genetic and in certain extent enzymatic control of antimutagenic action of vitamins at inducing mutations in E.coli cells, the foreign partner is needed to implement joint research.

This had the following main objectives:

1) To study the genetic control of antimutagenic action of vitamins, in particular, participation in the control recA, lexA dependent cell functions.

2) To analyze the dependence of antimutagenic effect of vitamins on the E.coli cell growth phases (stationary, logarithmic), which affects on the efficiency ratio of the direct alkylation and selective mutation in chromosome replication fork.

3) To study the role of various DNA polymerases types in anti-mutagenic action of vitamins and other biologically active substances.

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