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ANTIMUTAGENS OF DIHYDROPYRIDINE SERIES – TRIGGERS OF DEFENCE REACTIONS OF CELL AND ORGANISM AGAINST ENVIRONMENTAL MUTAGENS

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Effective antimutagens (AM) suppressing spontaneous and chemically induced mutagenesis in germ- and somatic cells of animals were revealed among 1,4-dihydropyridine derivatives. Effects of these compounds were detail studied in different test-systems that made it possible to establish peculiarities and some mechanisms of their action.

AM-treatment of drosophila larvae reduced the level of spontaneous mutations in male germ cells from 3 to 5 times and protected them against alkylating agent ethyl methanesulfonate (EMS). It should be noted that EMS was applied only to adult males. Nevertheless, AM-treatment at the larva stage prevented most effectively chemical mutagenesis in germ cells of adult individuals. When imago males were sequentially fed with AM and mutagen, protective effects were not observed. It follows from this that AMs do not interact with mutagen and most likely induce protective mechanisms reacting against a mutation process at its different stages. Suppression of EMS-mutagenesis and clastogenesis was proved to be due to the AM effect on DNA repair.

So, the effect of maternal repair of primary damages induced in mature spermatozoids was studied, and AMs were shown to increase accuracy of this process. Characteristically, level of chromosome breaks reduction was observed within two-week storage of mutagenized spermatozoids in females, i.e. not only in the presence but also for lack of AM in maternal organism. Some preparations of this group reduced the level of EMS-induced chromosome damages in bone marrow cells of mice. The relationship between the efficiency of antimutagen effect and the physiological state of animals was revealed. The same AM dose was found to decrease the maximum frequency

of EMS-induced micronuclear cells by 30% in males and by 70% in pregnant females. Protective effect did not manifest itself in fetuses. The data obtained are quite explainable if one assume that targets of the AM effect are endogenous protective systems, the least developed in fetuses and whose efficiency increases during pregnancy.
AM addition to fodder of carp from radiocontaminated ponds improved substantially productivity parameters of stripped fishes and decreased the frequency of chromosome aberrations and morphological malformations in their progenies. AM affected the developmental process in carp fry not only during feeding, but also for some weeks after its termination.

Thus, the AMs studied affect mediately activating some or other defense mechanisms. This “trigger” effect may be associated with control of appropriate gene expression.