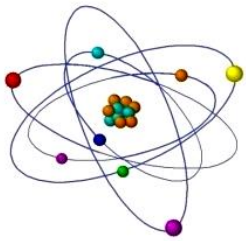
THE ACTION OF BIOLOGICALLY ACTIVE ADDITIVES ON THE FORMATION OF DISTANT RADIOBIOLOGICAL EFFECTS



Gogebashvili M.E., Ivanishvili N. I., Kiparoidze S. D., Kontselidze A. E.
Ivane Beritashvili Center of Experimental Biomedicine, Laboratory of Radiation Safety Problems

ABSTRACT
The paper discusses the risks caused by the use of biologically active additives in radiotherapy and diagnostics in terms of radiation safety. Their inclusion in the treatment methodology is an acute biomedical problem due to the unforeseen negative effects of their interaction with other pharmacological drugs. It has been concluded that insufficient study of the risks of using BAAs with different radiological methods can pose a serious threat to the patient's health and life.

Key words: Biologically Active Additives, gamma- irradiation, distant radiobiological effects

INTRODUCTION

The development of innovative medical technologies related to various types of radiation requires constant updating of our knowledge in the field of radiation safety. In addition to this, it is becoming especially necessary to carry out studies based on the fundamental radiobiological patterns established in specialized centers [1-4]. However, due to numerous reorganizations, the number of such centers in Georgia has significantly decreased. At the same time, scientific centers and commercial structures are functioning, where the solution of radiobiological tasks is led by specialists in neighboring fields. It is clear that in some cases, this circumstance can lead to the formation of a false direction and distortion of the laws of scientific discipline, so the realization of the data in such publications poses significant risks both in the processing of biomedical technologies and in predicting the risks of their use [5]. Recently this has been associated with a significant increase in biologically active additives (BAA) in the pharmaceutical market. It is known that unlike medicines, BAAs are used in healthy people and rarely for medicinal purposes [6-7]; In the latter case, their use is associated with certain risks, namely: 1) low level of study of their effects on the body; 2) dangers of overdose; 3) unforeseen adverse effects of interaction with other pharmacological drugs involved in the treatment methodology. Given the above, the study of limiting factors for the use of BAAs, especially in the presence of radiological clinical methodology, is an acute biomedical problem.

MATERIALS AND METHODS

For the study of distant effects, we propose a model based on in vitro irradiation of plant stem cells and the study of chromosomal aberrations in them. This choice was due to the fact that most of the buds on the market are based on plant material. Typically, they contain plant-specific secondary metabolites - phenolic compounds, terpenoids, alkaloids, glycosides, as well as antioxidants - tocopherol, ascorbic acid, carotenoids, polyphenols. All of these substances are involved in the detoxification of oxygen forms mainly in the membrane and cytoplasm. For tissue culture, we used the Murashige-Skoog cultural medium, in which the phytohormonal composition was gradually changed before and after irradiation. In vitro tissues were irradiated at 1-10 Gy dose intervals on a"gamma-capsule-2" irradiation device with a radioisotope of ^{137}Cs at a dose rate of 1.1 Gy/ min.
White mice of standard, homogeneous populations were used to study the effect of biologically

gamma-radiation dose of 4.5 Gy was used. The criterion in the analysis of distant radiobiological ffects was the average life expectancy. Analyzes were performed on control and experimental groups of animals. Each group included 30 animals. The control group was represented by non-irradiated mice that were in similar conditions as the experimental animals. One part of the experimental animals was fed saturated food with antioxidant mixture of multivitamins for 10 days before irradiation, while the other part was subjected to the usual food ration. Irradiation was performed at a dose of 4.5 Gy.

RESULTS AND DISCUSSION

Decreased functional, structural, and metabolic activity characteristics of cells and tissues are known to be one of the primary indicators of the condition of living objects when exposed to radiation. In this regard, the relationship between functional state processes and the level of radioresistance is an important criterion that determines the entire subsequent period of post-radiation recovery of the organism; however, substantiating the interrelationships of these systems through experiments has some methodological difficulties. Therefore, in order to influence the multifunctional regulatory system, we used in vitro cultural callus tissue, in particular, phytohormonal compounds, through which it is possible to have a complex effect on the functional and metabolic activity of the study tissues.

Model experiments on plant stem cells of D.stramonium have shown that the phytohormonal compounds we use, which are used for modeling substances of secondary metabolism, along with radiation, increase the probability of aberrations in cells. As can be seen from the first graph presented, the impact of growth-regulating substances (cytokinins - stimulate proliferative activity in tissues) during pre-radiation exposure on the tissue increases the likelihood of cytogenetic disturbances, while exposure to the same substances during the post-radiation period significantlyreduces radiation damage.

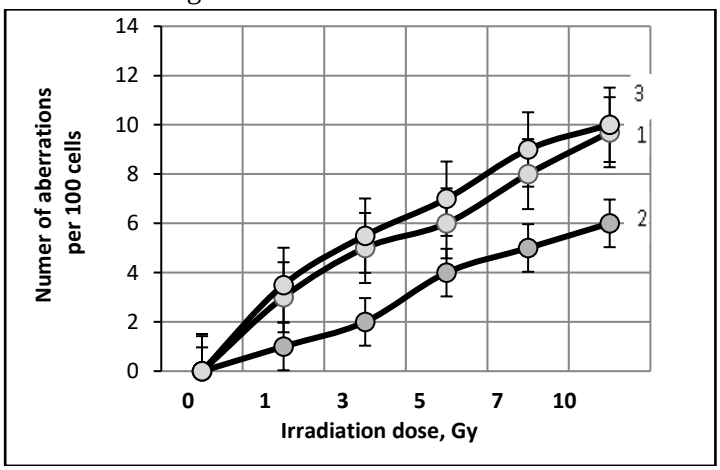


Fig.1. Influence of natural phytohormonal compounds on the number of chromosomal aberrations in irradiated stem cells (*in vitro*)

1. Chromosomal aberrations (complete phytohormonal medium); 2. Phytohormonal post-radiation action (using cytokines only); 3. Phytohormonal pre-radiation action (using cytokines only).

Model experiments have shown that the phytohormonal compounds used, which have the ability ofdamage in cells when exposed to radiation (Fig. 1). As can be seen from the picture, the main factormodeling the action of compounds of secondary metabolism, increase the likelihood of geneticis pre-radiation action, which determines the functional and metabolic state of tissues during radiationexposure. To confirm this view, we conducted a study on laboratory white mice.

Along the mice control group, a group fed with a mixture of multivitamins and antioxidants soaked in standard food for one week before irradiation was used. The data presented in Figure 2 show the regularity of the tendency to decrease the average life expectancy of the test animals when exposed to a pre-radiation regime of a mixture of multivitamins and antioxidants (Fig. 2-2), compared to the standard feeding option irradiated with the same dose (Fig. 2-3). Considering the results obtained in the general context of radiation safety problems, we can conclude that the issue of determining and standardizing the use of biologically active additives during radiation exposure to the organism has not been sufficiently studied.This is evidenced by data from recent clinical trials. In particular, it has been shown that taking dietary supplements during mammary glans's chemo- and radiotherapy increases the risk of relapse and death [8]. This includes food supplements that contain antioxidants and vitamins. It is believed that one of the ways of exposure to chemicals and radiation on pathological cells is oxidative stress, and antioxidants block this process, thus reducing the effectiveness of treatment. For this reason, it has been several years' doctors have been advising patients not to take antioxidants during therapy, although so far there has been no convincing scientific evidence to support this recommendation. Georgia is not an exception in this regard too, where there are no normative protocols for the use of biologically active supplements containing natural antioxidants. Despite a number of publications that have shown the dangers of misinterpreting the effects of some natural compounds during radiation exposure, the risks posed by this phenomenon still remain unnoticed. In this regard, the results of a study by American scientists who analyzed data on the lifestyle and prognosis of recovery of 1134 patients undergoing radiotherapy and chemotherapy. The researchers found that patients who received any antioxidants, including carotenoids, coenzyme Q10 and vitamins A, C, and E, at the beginning of chemotherapy and during chemotherapy, had a 41% higher risk of redeveloping breast cancer and 40% higher risk of death before the next observation, compared to the patients who excluded any supplements [8].

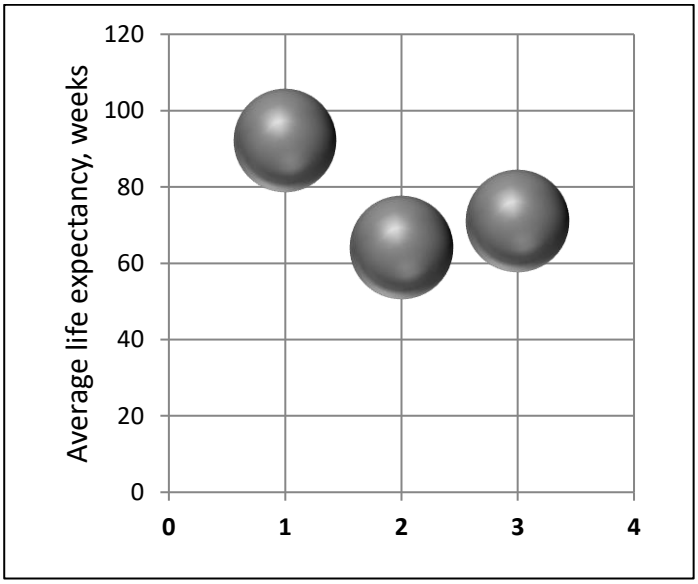


Fig.2. Impact of radiation exposure on the life span of white mice

1-control (non-irradiated); 2 - irradiation at a dose of 4.5-5 Gy under the influence of pre-radiation BAAs; 3 - irradiation at a dose of 4.5-5 Gy (the diameter of the figures in the diagram shows a 95% confidence interval).

CONCLUSION

Comparing the results obtained by us with the data of other studies, it becomes clear that insufficient study of the risks of using biologically active additives in combination with various radiological methods poses a serious threat to the health and life of patients. There is no doubt about the fact thatthe initial stage of treatment poses a serious threat in the form of distant post-radiation effects.

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