Prediction of Lethal Lesions after Exposure to Radiation and Hyperthermia

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Introduction

Many physical, chemical, biological and social factors may simultaneously exert their deleterious influence to men and the environment. The combined exposure to two harmful agents could result in a higher effect than expected from the addition of the separate exposures to individual agents. Therefore it is possible that, at least at high exposures, the combined effect of radiation with the other factor can be resulted in a greater overall risk. The basic assumption of synergism is that one sublesion produced, for instance, by ionizing radiation interacts with one sublesion from another environmental agent (for the specificity sake, let it be heat) to produce one additional lethal lesion. It would seem probable to suppose that the number of sublesions was directly proportional to the number of lethal lesions.

Materials and Methods

Zygosaccharomyces bailii (n), *Saccharomyces cerevisiae* (2n strains, XS800 and T1), *Endomyces magnusii* (2n). Cells were incubated before irradiation for 3-5 days at 30℃ on a complete nutrient agar layer to a stationary phase.

The ^{60}Co γ-ray source was a Gammacell 220 (AECL). The γ-ray dose-rate was 10 Gy/min.

Hyperthermia was given in a water bath where a desired temperature was maintained.

Theoretical Model for Synergy

Let *p1* and *p2* be the number of sublesions that occur for one lethal lesion induced by radiation and hyperthermia, respectively. Let *N1* and *N2* be the mean numbers of lethal lesions in a cell produced by these agents. A number of additional lesions *N3* arising from the interaction of ionizing radiation and hyperthermia sublesions may be written as

$$N3 = \min\{p1N1;\ p2N2\}. \qquad (1)$$

Here, $\min\{p1N1;\ p2N2\}$ is a minimal value from two variable quantities: *p1N1* and *p2N2*, which are the mean number of sublesions produced by ionizing radiation and hyperthermia, respectively. Thus, the model describes the mean yield of lethal lesions per cell as a function of ionizing radiation (*N1*), hyperthermia (*N2*), and interaction ($\min\{p1N1;\ p2N2\}$) lethal lesions.

Results and Discussions

The experimental values of irreversible component were obtained for a simultaneous action of ionizing radiation (^{60}Co) and hyperthermia on diploid yeast cells Saccharomyces ellipsoideus, and the predicted values were given in Table 1. It is apparent that the cell ability to recover from radiation damage is inversely proportional to the temperature at which the exposure was delivered. Yeast cells exposed to ionizing radiation at 55℃ almost completely failed to be recovered. Table 1 also includes the ratio of N2/N1 estimated on the basis of a whole set of experimental data (not presented here). The basic parameters of the model (*p1*=3.07 and *p2*=2.54) have been evaluated from real experiments.

Table.1. Irreversible component of radiation damage (*K*) after a simultaneous action of radiation and heat on *S. ellipsoideus* (vini)

Temp. ℃	20	45	50	52.5	55
N2/N1	0	0.21	0.55	1.36	7.19
K exp.	0.41	0.51	0.75	0.84	0.91
K, Theo.	0.41	0.66	0.80	0.89	0.95

A theoretical model was built for synergistic interaction of two different agents, based on the supposition that synergism takes place due to the additional lethal lesions arisen from the interaction of sublesions induced by both agents. One sublesion caused by irradiation interacts with one sublesion produced by heat. This process goes until the sublesions of a less frequent type are used up. The model predicts the dependence of synergistic interaction on the ratio *N2/N1* of lethal lesions produced by every agent applied, the greatest value of the synergistic effect as well as the conditions under which it can be achieved. The degree of synergistic interaction was found to be dependent on the ratio of lethal damage (*N2/N1*) induced by the two agents applied. The synergistic interaction is not observed at any *N2/N1* ratios.

Conclusions

The model indicates that for a lower intensity of physical agents or a lower temperature must be used to provide the greatest synergy. Actually, any decrease in the intensity of physical agents would result in a increase of the duration of thermoradiation action to achieve the same absorbed dose. Therefore, the number of thermal sublesions will also increase resulting in the disruption of the condition at which the highest synergy should be observed. Hence, to preserve an optimal *N2/N1* ratio with any decrease in the dose rate (or the intensity of other agents) the exposure temperature should be decreased. For a long duration of interaction, which is important for problems of radiation protection, low intensities of deleterious environmental factors may, in principle, synergistically interact with each other or with an environmental heat.

REFERENCES

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