AN ANALYTICAL APPROACH TO THE COMPARISON OF CHEMICAL AND RADIATION HAZARDS TO MAN

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INTRODUCTION

The main hazards arising from the exposure to ionizing radiation are the so called late effects; the induction of cancer and of hereditary defects. However, there is an increasing awareness that many other environmental agents such as UVR and chemicals are mutagenic and potentially capable of causing cancer and hereditary defects. Thus, the effects caused by radiation are not unique and consequently it is illogical to place radiation in an exceptional position with respect to the protection of man. A comparison between radiation and other mutagenic agents depends on the availability of comparative analytical and assessment techniques. In this paper we present an analytical model, based on radiation biological concepts at the molecular level which permits an analysis of the effects of other agents and also predicts that a synergistic interaction between two different mutagenic agents can occur at the molecular level.

ANALYSIS

Figure 1 presents schematically the molecular mechanisms assumed to be responsible for biological effects such as cell death, aberrations and mutations. The molecular theory (1,2,3) assumes that radiation induced DNA double strand breaks are the crucial radiobiological lesions. The figure shows that double strand breaks have a linear - quadratic dose relationship, that UVR or a mutagenic chemical causing single strand lesions will have a quadratic exposure relationship and that the combined action of radiation and agent gives an additional contribution of double strand lesions arising from the interaction between a single strand break and a single strand lesion. The total number of lesions is

$$N_T = \quad D + \quad D^2 + \quad XD + \quad X^2 \qquad (1)$$

This predicts that for radiation curves the coefficient remains constant but combined treatment increases the linear coefficient (- + X). For agent curves the coefficient remains constant but combined treatment leads to a linear coefficient(D).

Figure 2 presents a series of radiation survival curves after a UVR pre-dose and a series of UVR survival curves after a radiation pre-dose. The analysis has been made according to equation (1), all radiation curves have the same coefficient, increases with increasing UVR pre-dose, all UVR curves have the same coefficient, the linear coefficient increases with radiation pre-dose.

Figure 3 presents the combination of radiation and BUdR on cell survival and chromosomal aberrations. Again the change in shape of the

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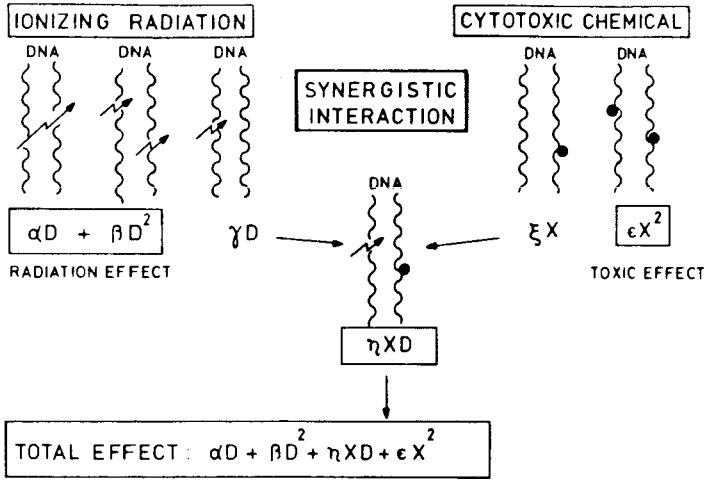

Figure 1. Schematic representation of the action of ionizing radiation, other mutagenic agents and the synergistic interaction between the two agents.

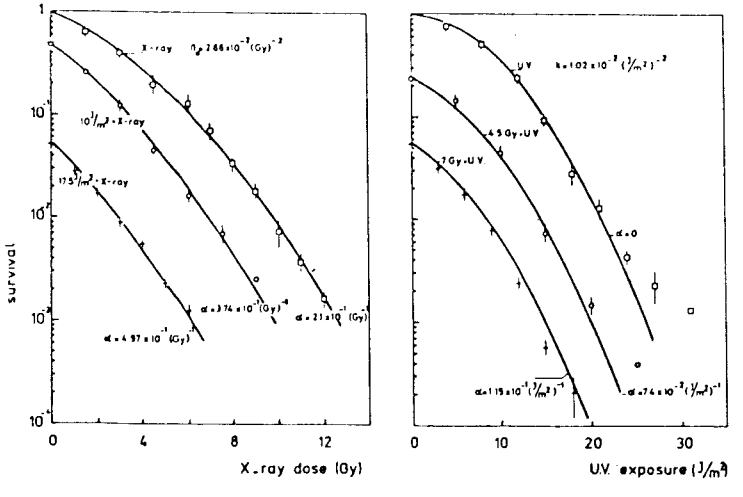

Figure 2. Survival of Chinese hamster cells for combined treatments of X-rays and UVR (4) analysed according to equation (1).

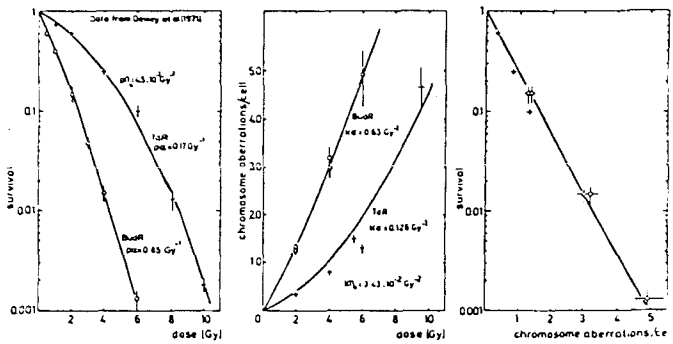

Figure 3. Survival and chromosomal aberrations induced by radiation in synchronised Chinese hamster cells with and without BUdR (5) analysed according to equation (1).

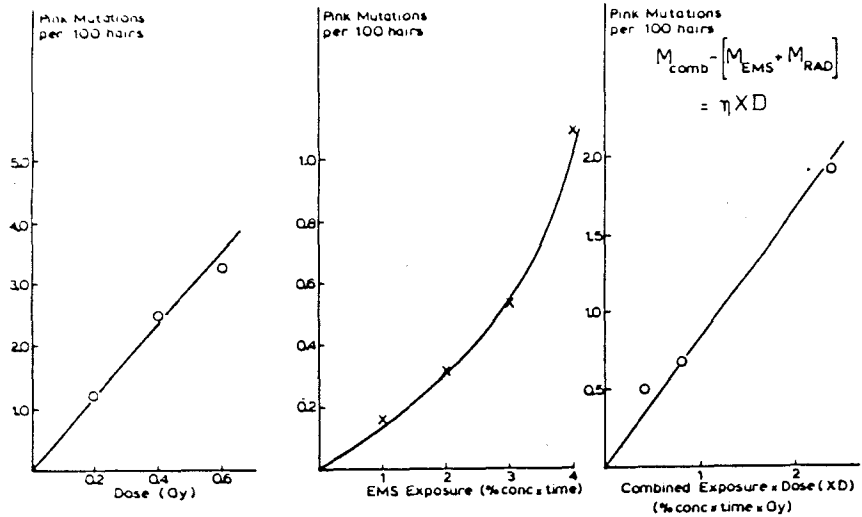

Figure 4. The induction of pink mutations in Tradescantia stamen hairs by X-rays and EMS (ethyl methane sulphonate) and the contribution of mutations arising from the interaction between the EMS and the X-rays as a function of the product of chemical exposure and radiation dose.

curves is reflected in a change in the linear coefficient only. The last part of the figure demonstrates that the change in survival is paralleled by the change in aberrations.

Figure 4 illustrates the effect of EMS and radiation on the induction of pink mutations in the stamen hairs of Tradescantia. The last part of this figure reveals that the difference between the combined treatment and the sum of the separate treatments is proportional with the product of chemical exposure and radiation dose(i.e. XD) as expected from equation (1).

CONCLUSIONS

1. The analysis shows that the synergistic interaction occurs at the molecular level in the DNA.
2. The synergism can be demonstrated in cell survival, chromosomal aberrations and somatic mutations and can therefore be expected forcancer and hereditary defects.
3. The synergistic interaction leads to an increase in the linear component of the radiation effect which is critical at low doses and important for radiological protection.
4. The model implies that a synergistic interaction between two different mutagenic chemicals can also be anticipated.
5. The model provides an analytical vehicle which can be used to compare the effects of radiation and other mutagenic agents at the mechanistic level.
6. If we are concerned to protect man from the increasing mutagenic, and thus carcinogenic load, an integral protection philosophy is essential.

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