TOXICITY OF SODIUM ASCORBATE AND ALLOXAN MONOHYDRATE TO 3T3 MOUSE CELLS

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Sodium ascorbate has been reported to be toxic to Ehrlich ascites carcinoma cells (Benade, Howard & Burk, 1969) and to SV40-transformed 3T3 cells (Cope, 1978). These data suggest that there is a cellular basis for the use of vitamin C in the treatment of cancer. In both types of cell, the ultimate cytotoxic agent was shown to be hydrogen peroxide, produced by oxidation of the ascorbate.

In the presence of oxygen, ascorbate and alloxan monohydrate produce three cytotoxic agents. Ascorbate reduces alloxan to dialuric acid and this reduced form is oxidised back to alloxan with the production of hydrogen peroxide, superoxide anions ($O_2^{\cdot -}$), and hydroxyl radicals ($\cdot OH$).

The experiments described show that concentrations of alloxan and ascorbate which are ineffective when either agent is administered separately are highly toxic when the two are administered together. Fig. 1 shows the effect of various concentrations of ascorbate and alloxan on cell number. It has been suggested that hydroxyl radical production is responsible for the diabetogenic properties of alloxan since hydroxyl radical scavengers, such as ethanol, prevent the development of diabetes in alloxan treated mice (Cohen & Heikkila, 1978). The toxic effect described above, however, is due primarily to hydrogen peroxide production since catalase protects the cells while superoxide dismutase and thiourea ($O_2^{\cdot -}$ and $\cdot OH$ scavengers respectively) have no protective effect.

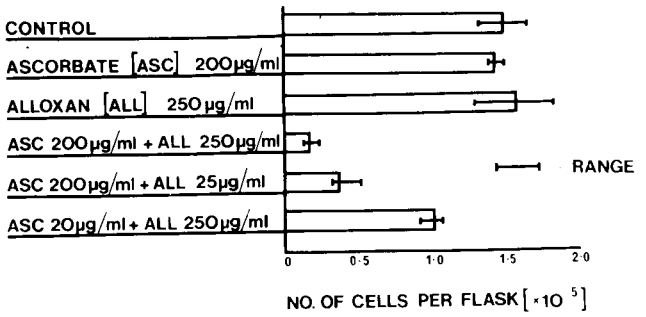

Figure 1. The effect of ascorbate and alloxan on cell number. The substances were added 3 hours after the cells had been seeded at 5 x 10^5 cells per flask in MEM + 10% FCS. The cells were counted 24 hours later. Each group contained three flasks.

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