VIDEOTAPE ILLUSTRATION OF CULTURED BEATING HEART CELLS AND THE APPLICATION OF SUCH CULTURES TO STUDYING THE CARDIOTOXICITY OF ADRIAMYCIN

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It is now recognised that microbiological studies, which were adequate for anti-bacterial antibiotics, are not adequate for anti-tumour antibiotics, but that additional mammalian cell studies are necessary (W.H.O. 1981).

This paper reports the use of cultures of beating heart cells to study precisely what cellular components are damaged by adriamycin.

A method of preparing consistently beating cells has already been described (Dawson & Abdul-Jabar 1980) and a preliminary report (Dawson et al, 1981) indicated that, at least in part, heart cell damage was brought about by superoxide radical which dismuted to hydrogen peroxide, which in turn could not be detoxified by heart cells because of their low levels of catalase.

It was considered likely that ATPase might be involved since it is situated in the type of cell junctions found in heart tissue. ATP (0.8 μg/flask) decreased beating rate. Then 1 μg/flask increased the rate and finally 10 μg/flask stopped beating altogether. The volumes of medium per flask were in all cases 3 ml. ATP (8μg/flask) along with the adriamycin protected beating. Further evidence of a role for ATPase in this reaction was found from the fact that ouabain (400 μg/flask), which specifically binds to ATPase and inhibits it, increased the toxicity of adriamycin.

Alternatively, lipid peroxidation has been suggested as the nature of adriamycin damage (Myers et al 1977). However in our system we were unable to detect any malondialdehyde. This does not totally rule out this type of damage, as the substance may have been produced in amounts too small to detect by available means. That lipid may be affected is indicated by the fact that α-tocopherol (300 μg/flask), a lipid-soluble substance, gave some protection against adriamycin. However, this was less when used alone than when in combination with ATP.

The toxicity of adriamycin to a line of cultured malignant epithelial cells was also investigated, and found not to be reduced by superoxide dismutase + catalase or by α-tocopherol. This shows that reduction of cardiotoxicity can be achieved without lessening the required effect.

W.H.O. Expert Committee on Biological Standardization, 31st Report, Tech. Rep. Ser. 658, Geneva, 1981
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