STUDY ON CYTOTOXICITY OF TRICHOTHECENES IN CULTURE CELLS *IN VITRO*

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ABSTRACT

Cytotoxic effect of trichothecenes was investigated in two types of culture cells, AS-30D and TA-3. The experiments were designed to determine the primary site of action and the possible mechanism of trichothecenes leading to cell death. Trichothecenes, regardless of types, exhibited cytotoxic effect and the damage of cell injury was proportional to the concentration of toxins. In the present study, the mechanism of action that trichothecenes led to cell damage is proposed by the hypothesis that trichothecenes may act as calcium ionophore which induce influx of calcium to, the target site, plasma membrane. The elevated cellular calcium concentration was followed by phospholipase activation in plasma membrane which intensified impairment of membrane and cellular function leading to cell injury. The mechanism could be successively supported by enhance influx of calcium to cell observed as early as 5 min. of toxin exposure period. The leakage of cellular enzymes : AST, ALT, ALP and LDH, as the index of plasma membrane damage was later found approximately 10 min. after the exposure. The occurrence was followed by the observation of dye

stained damage cells after 15 min. of toxin exposure. In addition, the reduction of energy charge system after 10 min. exposure indicated the impairment of cellular function as the consequence from plasma membrane damage. Hence, the sequence correlation and the similar pattern observed in both cell systems supported the possibility of this overall mechanism of trichothecene-induced cytotoxicity. These cytotoxic appearance was effectively protected by the anti-inflammatory steriod, dexamethasone, which acted as phospholipase inhibitor. The experimental data emphasize the mechanism of cytotoxicity with the disturbance in calcium homeostasis and provide further insight into the toxicological sequence provoked by trichothecenes which can be protected by dexamethasone.