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Yvonne Morris

Abstract

Research Project
The project undertaken involved a study of the effects of the inhibitor N-methyl isatin thiosemicarbazone (Marboran) on the replication cycle of cowpox virus in monolayers of baby hamster kidney cells (BHK). The cytotoxic effects of Marboran on the BHK cells were studied and were found to be directly related to the time of exposure to the inhibitor with a maximum tolerated dose of Marboran of 30/UM/ml. after 7 days. This drug concentration was subsequently used to avoid the occurrence of a cytotoxic effect of Marboran masking any cytopathic effect (CPE) of the virus when both inhibitor and virus were used in conjunction.

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RESEARCH PROJECTS

STUDY OF THE INHIBITORY ACTION OF MARBORAN ON THE REPLICATION CYCLE OF COWPOX VIRUS

Yvonne Morris

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A study of the replication cycle of cowpox in BHK tube culture yielded one-step growth curves for extracellular virus, cell-associated virus (CAV) and total virus. Infected tube cultures with no added inhibitor were used as experimental controls producing normal one-step growth curves for CAV, the virus titre reaching a maximum of $10^{-3.3}$ 24 hours after infection. The eclipse phase was found to last approximately 10 hours by which time the virus time had risen to that of the original inoculum. Maximum inhibitia of replication occurred when Marboran was introduced to cultures 2 hours post-infection, the virus titre having fallen from the normal virus growth curve value of $10^{3.3}$ to $10^{1.33}$. It was apparent from the results that, when inhibitor was used, there seemed to be a prolongation of the eclipse phase since titres took as long as 24 hours to reach the initial inoculum level of $10^{1.6}$.

From the results obtained it seemed that Marboran in some way interfered with the M-RNA responsible for the synthesis of "late" proteins which include those structured proteins necessary for viral maturation. Further support has been given to this theory by studies of the cytological changes occurring in coverslip monolayers of BMK cells when infected with (a) cowpox virus alone and (b) with virus treated with 30 μM/ml. Marboran. The development of "B" and "A" type inclusions was shown to occur in both (a) and (b). Since, therefore, the Marboran had no effect on the development of the "B" inclusions which are associated with "early" protein and DNA synthesis, the inhibitor would apparently be acting later in the replication cycle.

There is some evidence, however, that the inhibitor may act earlier. The fact that maximum inhibition occurred when Marboran was added 2 hours post-infection may be significant.

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