EFFECT OF *CROTALUS* VENOM ON GROWTH OF MEASLES VIRUS

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Introduction. The processes leading to the initiation of cells infection with virus are complex and they can be divided into at least two stages. While the first stage, the virus binds to receptors on the cell surface, the other stage, occurs an internalization of the virus and subsequent initiation of the virus replicative cycle. The adsorption and penetration events require glycoprotein encoded by the viral genome. Measles virus (MV) present two viral glycoprotein that serve as a cellular receptor for MV and accelerating the penetration of the virus into host cells (1). The removal of glycoprotein from the cell membrane by using proteolytic enzymes could inhibit the penetration of MV into host cells. In this study, the effect of *Crotalus d. terrificus* venom (Cdt) on different steps of the replicative cycle of MV was studied.

Methodology. MV from Edmonston strain virus and Cdt was obtained from Instituto Butantan. Groups of VERO cells in L-15 medium plus 5% FBS were cultured and incubated in at 5% CO_2 and 37°C. Different amounts of Cdt were added to cells and incubated for 3h. The supernatants were removed and determined the cytotoxicity and viability. Separated groups of cells were infected with MV at different multiplicity of infection (moi). The cultures infected with MV for different times of venom treatment were incubated in at 5% CO_2 and 37°C for 5 days. MV titres in the cell cultures were expressed as plaque formation unit (PFU).

Results and Discussion. The influence of the Cdt on the cytotoxicity and viability of the VERO cells was studied. The cells were sensitive to the Cdt treatment in a dose-dependent manner, at 0.1 µg/ml did not induce cytotoxic effect. In contrast, Cdt at 1 to 1000 µg/ml was able to induce an increase of cytotoxic and staining cells.

A series of the experiments are described showed that the Cdt also had antiviral activity against MV in VERO cells. Confluent cells were treated with different amounts of Cdt and infected with MV. As shown in Figure 1 Cdt inhibited the MV adsorption and penetration. In one-step growth cycle assays Cdt prevented the MV adsorption in a dose-dependent manner.

VERO cells were treated with 1 µg/ml of venom at different times and infected with 10 moi of MV. Figure 2 shows that the MV yield was 10 and 75% in cultures treated with Cdt. The inhibition was also observed, particularly when the Cdt was added in the first one hour before or during MV infection.

Figure 1. Percentage of inhibition of MV growth.

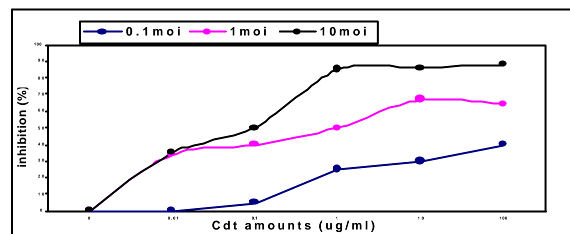
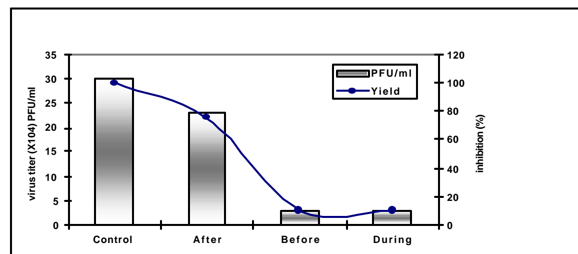


Figure 2. Effect of venom on MV yield.



Conclusions. This study clearly demonstrated that Cdt presented a significant antiviral activity to MV. Cdt was tested on different steps of the replicative cycle of MV as shown by virus yield reduction. Moreover, it was necessary determine the conditions for obtaining a decrease on the virus growth after treatment with venom. Under one-step growth conditions, the treatment of cells with Cdt during/1h before of the MV infection showed to inhibit the virus adsorption and/or penetration by around 90%. This inhibitory action was not due to a virucidal effect. However, the mechanism of the antiviral effect is still not known.

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