Antiviral potency of an extract from *Nerium oleander*

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INTRODUCTION

Targeting of multiple viral replicative steps with a single therapeutic is a highly coveted goal. Recent approaches using chimeric antibodies with dual specificities have demonstrated therapeutic efficacy in murine models against EBOV and SUDV, with extended efficacy against SUDV. TAVF and RESTV in vivo. The breadth of efficacy, however, is still constrained by geno as efficacy against EBOV/Bolivian lineage viruses and Maguari strains. PBI-05204 is a cardiac glycoside-containing extract from *Nerium oleander* that has shown antiviral efficacy and is a cancer therapeutic in clinical trials. PBI-05204 and oleandrin, a cardiac glycoside that is one of the major therapeutic agents in the PBI-05204 extract, are assessed for antiviral efficacy.

OBJECTIVES

Assess broad spectrum potency of extract from *Nerium oleander*.

BACKGROUND

Cardiac glycosides are used therapeutically to correct irregular heart rhythms and congestive heart failure. The cardiac glycoside oleandrin, as well as an oleandrin-containing extract of *Nerium oleander* known as PBI-05204, have also been shown to have antitumor potency in vitro and in vivo. Furthermore, PBI-05204 has been used in phase I and II clinical trials against solid tumors and did not result in any significant cardiotoxicity. Interestingly, oleandrin contained within the PBI-05204 extract has been shown to cross the blood-brain barrier in mouse models. Recent studies have uncovered potential roles for cardiac glycosides as antiviral drugs against HIV, CMV and HSV through a variety of mechanisms. Cardiac glycosides disrupt cellular Na+-K+-ATPase, an enzyme that is essential for maintaining the intracellular homeostasis of calcium in smooth muscle cells in the heart by regulating the flow of sodium and potassium ions. Depressed Na+-K+-ATPase activity therefore leads to dysregulated calcium channel function. The indirect inhibition of calcium regulation by cardiac glycosides suggests that these drugs may also be effective against flaviviruses as calcium channel blockers have demonstrated efficacy against flavivirus. Calcium channel blockers have been demonstrated to mitigate their antiviral effect by inhibiting new virus particle formation.

MATERIALS AND METHODS

A defined extract from *Nerium oleander* and purified oleandrin were used to pretreat Vero cells prior to and post-infection with MARV and BDBV. An immunofluorescence assay was used to determine antiviral efficacy 48 hr post-infection. For passaging experiments, Vero cells were infected in the presence of PBI-05204 or oleandrin. Supernatant was collected 48 hr later. The supernatants were then passaged onto fresh Vero cells for the presence of infectious virus. An EBOV minigenome was used to assess viral transcription and replication in the presence of PBI-05204 or oleandrin.

RESULTS

PBI-05204 and oleandrin fully inhibited MARV and EBOV infection in Vero cells. No infectious progeny virus was recovered from supernatants of cells infected with EBOV or MARV when treated with PBI-05204 or oleandrin. Neither virus transcription or replication were inhibited by treatment with PBI-05204 or oleandrin, indicating the inhibition does appear to be linked to viral polymerase function.

DISCUSSION

The broad spectrum efficacy we’ve presented may be especially critical as certain therapeutic elements within the PBI-05204 botanical drug can be found to accumulate in the CNS, which is essential for viruses that have demonstrated neurotropic effects.

CONCLUSION

Our observations, conclusion and recommendations are those of the author and are not necessarily endorsed by the U.S. Army.

REFERENCES