Antiviral activity of *Carica papaya* extract against experimental dengue virus 1 infection

MO Galappaththi, WMA Indeewari, AMSB Abeykoon, MGCM Muthuwaththa, VK Kothwela, AHMLN Kumari, HDRPD Harasgama, F Noordeen

Introduction

Dengue is a major public health problem in tropical countries including Sri Lanka. There are no specific antiviral drugs or an effective vaccine available against dengue as yet. Plant derived compounds are an important option for development of new drugs. *Carica papaya* of the family *Caricaceae* is a traditionally used medicinal plant to treat dengue. The objective of this research was to determine the antiviral activity of *C. papaya* leaf extracts against dengue virus-1 (DENV-1). As a first step of exploring the antiviral activity, the cytopathic effects of the *C. papaya* leaf extract was done to select a minimum toxic concentration against the experimental DENV-1 infection in C6/36 cells.

Methods

First, *C. papaya* leaf extract was prepared in two-fold dilution series from neat to 1/1024. Then, two 24-well cell culture plates containing C6/36 cells infected with DENV-1 were treated with *C.papaya* leaf extracts at different concentrations. The cells were then harvested with the supernatant for testing. Viral RNA extracted (QIAGEN, Germany) from DENV-1 infected untreated control and four infected treated samples with *C. papaya* leaf extracts were subjected to the qRT-PCR. The analytical system based negative control, positive control and four standard dilutions of positive control in replicates were used for quantifying the DENV-1 RNA using the Dengue generic real time RT-PCR (Liferiver, China) with an analytical sensitivity of $1x10^3$ copies/ mL.

Results

According to cell morphology, less damage was observed in 1/16 – 1/512 *C. papaya* leaf extract dilutions. Thus 1/32- 1/256 dilutions were selected for treating the experimental DENV-1 infection. qRT-PCR showed DENV RNA in all 4 standards controls (SD1-10^7, SD2-10^6, SD3-10^5, SD4-10^4 DENV copies/ mL), positive control ($5x10^7$ DENV copies/ mL) and DENV-1 infected untreated control ($3x10^4$ copies/ mL). qRT-PCR did not show DENV RNA in negative control and four DENV-1 treated samples with 4 different concentrations of *C. papaya* leaf extracts.

Conclusions

According to qRT-PCR results, DENV-1 infection is inhibited by treatment with *C. papaya* extract in all four concentrations tested in the current experiment. This data suggests the potential of *C. papaya* leaf extract for future development of anti-viral drugs against DENV-1. Experiments are in progress to test *C. papaya* leaf extract against DENV-2, DENV-3 and DENV-4.

Keywords: *Antiviral activity, C. papayaleaf extract, DENV-1 infection, qRT-PCR*

Funding: University of Peradeniya (*Grant No* URG/2016/47/M)

Department of Microbiology, Faculty of Medicine, University of Peradeniya, Peradeniya, Sri Lanka
Address for correspondence: Prof Faseeha Noordeen. Telephone: +94772293301
Email: faseeha.noordeen12@gmail.com *https://orcid.org/0000-0002-2018-0606*