The in vivo antiviral activity of the anti-hepatitis C virus drugs daclatasvir and sofosbuvir against SARS-CoV-2

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Background

The SARS-CoV-2 pandemic continues to cause major global morbidity, mortality and economic burden. The public health urgency led to the study of already approved drugs as repurposed medicines to treat individuals with COVID-19. This approach has proven successful to date. The understanding of preclinical activity, mechanism of action, pharmacokinetics and safety are critical for achieving clinical benefit. Based on re-purposing.

Drug-screening systems (DSSs) against hepatitis C virus (HCV) have shown a decrease in viral titers, decreased replication in cell culture supernatant was measured by plaque assay. (B) Next, Calu-3 cells were infected at a MOI 10 times higher than used in other experiments, 0.1, and sequentially treated with sub-EC10 concentrations of sofosbuvir (SFV) or daclatasvir (DCV). The viral RNA was unbiased sequenced using a MGI thermocycler and the respective phylogenetic trees were visualized (C) and the different nucleotide substitutions were highlighted on the RNA genome of SARS-CoV-2 (D).

Figure 4. Schedule (SIP) inhibits SARS-CoV-2 replication in human F2 and human Vero cells-derived NSCs infected with SARS-CoV-2. (A) NSCs were infected at MOIs of 0.1 and treated with 1 µM of SFV or daclatasvir (DCV) and the clinical samples were harvested. (B) Next, Calu-3 cells were infected at a MOI 10 times higher than used in other experiments, 0.1, and sequentially treated with different concentrations of daclatasvir (DCV) and sofosbuvir (SFV) and the viral RNA was unbiased sequenced using a MGI thermocycler. The RNA sequences generated at different concentration levels of the drugs were compared against the SARS-CoV-2 genome and the sequences of the respective replicating virus (E).

Results

DCCV is more potent than SFV to inhibit the production of infectious SARS-Cov-2 particles

Resumed Methodology: Inhibition assays were performed at MOI of 0.01 for Vero cells 24 h after infection, and 0.1 for Huh-7 and Calu-3 cells 48 h after infection. Culture was treated after the infection period and cell culture supernatant fractions were harvested. After RNA extraction, the viral RNA was quantified by RT-qPCR.

Table 1. The pharmacological parameters of SARS-CoV-2 infected cell.

Table 2. The percentage of wild type, derivative (A) and normalized (B) reports are presented. (C) the scheme represent the different concentrations of the drugs, and its effect on the relative reduction of SARS-CoV-2 RNA (black dot). The virus was inhibited in Vero cells at 0.1 and Calu-3 at 0.01 MOI, with daclatasvir and sofosbuvir.

Conclusions

About this, our data reveal that SFV and DCCV inhibited SARS-CoV-2 replication in physiologically relevant cells, including hepatic and ileal mot盶es. Besides, the drugs prevented virus-induced mortality in the experimental system. The SARS-CoV-2 RNA was quantified by RT-qPCR, measurement of its RNA levels in the culture supernatant was measured by plaque assay. (B) Next, Calu-3 cells were infected at a MOI 10 times higher than used in other experiments, 0.1, and sequentially treated with sub-EC10 concentrations of sofosbuvir (SFV) or daclatasvir (DCV) and the RNA sequences generated at different concentration levels of the drugs were compared against the SARS-CoV-2 genome and the sequences of the respective replicating virus (C). DCCV provided a significant antiviral effect when compared to SFV, and the different nucleotide substitutions were highlighted on the RNA genome of SARS-CoV-2 (D).

Figure 3. Schedule (SIP) inhibits SARS-CoV-2 replication in human F2 and human Vero cells-derived NSCs infected with SARS-CoV-2. (A) NSCs were infected at MOIs of 0.1 and treated with 1 µM of SFV or daclatasvir (DCV) and the clinical samples were harvested. (B) Next, Calu-3 cells were infected at a MOI 10 times higher than used in other experiments, 0.1, and sequentially treated with different concentrations of daclatasvir (DCV) and sofosbuvir (SFV) and the viral RNA was unbiased sequenced using a MGI thermocycler. The RNA sequences generated at different concentration levels of the drugs were compared against the SARS-CoV-2 genome and the sequences of the respective replicating virus (C). DCCV provided a significant antiviral effect when compared to SFV, and the different nucleotide substitutions were highlighted on the RNA genome of SARS-CoV-2 (D).