



Antiviral activity of glucose-derived reactive metabolite, methylglyoxal against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

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ABSTRACT

Background: The ongoing coronavirus disease 2019 (COVID-19) pandemic has resulted in a global health emergency. With incomplete vaccination and incomplete protection of the vaccinated population, there remains an urgent need to develop drugs to treat COVID-19. Our previous *in silico* analysis suggested vulnerability of SARS-CoV-2 to inactivation by the endogenous reactive metabolite, methylglyoxal (MG), by modification of arginine residues in the functional domains of viral spike and nucleocapsid proteins¹⁻³. In this study, the antiviral activity of MG against wild-type SARS-CoV-2 using *in vitro* assays was evaluated.

Methods: Wild-type SARS-CoV-2 with titers of multiplicities of infection (MOI) 0.8, 0.2, 0.02, and 0.01 were incubated with 2-fold serial dilutions of MG (7.8 μM to 500 μM) in infection medium for six hour. MG-treated and untreated control SARS-CoV-2 were incubated with confluent cultures of Vero cells *in vitro* for one hour, cultures were washed and then incubated in a fresh infection medium at 37°C for 4 - 5 days until 70% of virus-infected cells displayed cytopathic effect (CPE). The antiviral activity of MG was judged by assessing virus replication using quantitative reverse transcriptase-polymerase chain reaction (RT-PCR) and median tissue culture infectious dose (TCID₅₀) assays.

Results: MG inhibited virus replication as measured by PCR and CPE of SARS-CoV-2 *in vitro*, with TCID₅₀ increasing with increasing MOI. MG was most potent at MOI 0.02 and 0.01 where EC₅₀ of MG was 49.6 \pm 4.7 μM and 28.5 \pm 1.3 μM ; respectively. Similar findings were also found for a shorter incubation period (3 hours) of MG and virus.

Conclusion: MG has inhibitory activity against wild-type SARS-CoV-2 for virus exposure in the cell-free systems at low MOI. However, the antiviral activity of MG against other SARS-CoV-2 variants including alpha- and beta-variants is being investigated. Drugs increasing cellular concentration of MG to viricidal levels may have anti-COVID-19 activity.

Keywords: SARS-CoV-2, COVID-19, methylglyoxal, antiviral.

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