

Dear Editor,

Will you please consider the manuscript headed "*In vitro* Evaluation of the Antiviral Activity of Repurposable Drugs against SARS-CoV-2: Methylene Blue", for publication in Clinical Infectious Diseases as major article in the special issue "Management of infections at the University Hospital Institute Méditerranée Infection: the Covid-19 paradigm".

All authors confirm that the Advice to Contributors has been read and accept the conditions set down therein. All the authors have seen and approved the manuscript and contributed significantly to the work. The manuscript has not been previously published nor is being considered for publication elsewhere.

This manuscript reported the high *in vitro* antiviral activity of methylene blue against infected Vero E6 cells with two clinically isolated SARS-CoV-2 strains (IHUMI-3 and IHUMI-6). The median effective concentration (EC₅₀) and 90% effective concentration (EC₉₀) of methylene blue against IHUMI-3 were $0.41 \pm 0.34 \mu\text{M}$ and $1.85 \pm 1.41 \mu\text{M}$, respectively; and $1.06 \pm 0.46 \mu\text{M}$ and $5.68 \pm 1.83 \mu\text{M}$ against IHUMI-6. Methylene blue interacted at both entry and post-entry stages of SARS-CoV-2 infection in Vero E6 cells as retrieved for hydroxychloroquine. The effects of methylene blue were additive with those of quinine, mefloquine and pyronaridine.

Best regards

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