# Impact of SARS-CoV-2 infection (COVID-19) on cytochromes P450 activity assessed by the Geneva cocktail.

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April 16, 2024

## Abstract

Background and purpose Coronavirus Disease 2019 (COVID-19), caused by SARS-CoV-2 infection, is a severe acute respiratory syndrome with an underlying inflammatory state. We have previously demonstrated that acute inflammation modulates cytochromes P450 (CYP) activities in an isoform-specific manner. We therefore hypothesized that COVID-19 might also impact CYP activities, and thus aimed to evaluate the impact of acute inflammation in the context of SARS-CoV-2 infection on the six main human CYPs activity. Experimental Approach This prospective observational study was conducted in 28 patients hospitalized at the Geneva University Hospitals (Switzerland) with a diagnosis of moderate to severe COVID-19. They received the Geneva phenotyping cocktail orally during the first 72h of hospitalization and after three months. Capillary blood samples were collected 2h after cocktail administration to assess the metabolic ratios (MRs) of CYP1A2, 2B6, 2C9, 2C19, 2D6 and 3A. CRP, IL-6 and TNF-α levels were also measured in blood. Key Results CYP1A2, CYP2C19, and CYP3A MRs decreased by 52.6% (p=0.0001), 74.7% (p=0.0006) and 22.8% (p=0.045), respectively, in COVID-19 patients. CYP2B6 and CYP2C9 MRs increased by 101.1% (p=0.009) and 55.8% (p=0.0006) respectively. CYP2D6 MRs variation did not reach statistical significance (p=0.072). As expected, COVID-19 was a good acute inflammation model as mean serum levels of CRP, IL-6 and TNF-α were significantly (p<0.001) higher during SARS-CoV-2 infection. Conclusion and implications CYP activities are modulated in an isoform-specific manner by SARS-CoV-2 infection. The pharmacokinetics of CYP substrates, whether used to treat the disease or as the usual treatment of patients, could be therefore clinically impacted.

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