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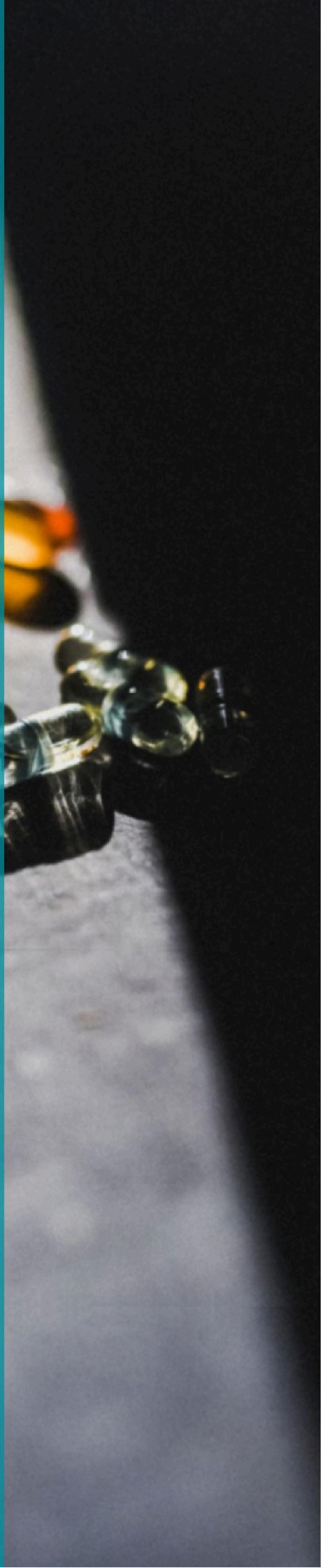

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Umbrella review on the possible use of Ivermectin in the treatment of COVID-19

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Background: The urgency to find treatment and prophylactic measures for COVID-19, motivated the use of drugs usually indicated in other pathologies, such as Ivermectin (commonly used as antiparasitic). **Objective:** The main objective of this study was to evaluate the potential use of ivermectin in the treatment of COVID-19, and to identify its mechanism of action and dosing regimen regarding this particular indication. **Methods:** To perform this umbrella review, a bibliographic search was carried out in the Pubmed, LILACS, SciELO and Wiley Online Library databases using the terms "Ivermectin AND COVID-19" and "Ivermectin AND SARS-CoV-2". Only articles published between January 2020 and March 2022 written in English or Portuguese and configured in review or meta-analysis formats, were considered. The selection of the articles returned in the initial search (n=1609), resulted from the analysis of the titles and abstracts, and was performed after elimination of duplicates. Studies addressing the pharmacology, pharmacokinetics and/or pharmacotherapy of ivermectin in the treatment of COVID-19 were considered eligible. **Results:** Twenty-six articles that met the inclusion criteria were selected. In patients with COVID-19, Ivermectin presented as main clinical result a decrease in mortality. Although there are several proposed mechanisms, the antiviral mechanism against SARS-COV-2 may be multimodal. Some of the studies demonstrated that the IC50 value of Ivermectin required to inhibit the replication process of the SARS-CoV-2 virus is much higher than the maximum plasma concentration reached after administration of approved doses. However, administration via inhalation or with nanotechnology may be promising, according to some reviews, as it would increase the concentration of ivermectin at the site of action. Preliminary studies using ivermectin in COVID-19 patients reported nausea, vomiting and increased circulating liver enzymes among the main side effects. The small samples used in the various studies and the nonspecification of the administered dose are the main limitations of human studies. **Conclusion:** Most reviews suggest that further studies are needed to prove that tolerable doses of ivermectin may be effective in the treatment of SARS-CoV-2. It should also be noted that the potential benefit associated with treatment with ivermectin does not outweigh or decrease the relevance of vaccination.

Keywords: COVID-19; ivermectin; pharmacotherapy; SARS-CoV-2;