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# Carvedilol and COVID-19: A Potential Role in Reducing Infectivity and Infection Severity of SARS-CoV-2



Dear Editor:

Angiotensin-converting enzyme 2 (ACE 2) is expressed by several cells in the body, like the epithelial cells of the lungs and the blood vessels. It is a host receptor for severe acute respiratory syndrome coronavirus [SARS-CoV] and SARSCoV-2.<sup>1</sup> ACE inhibitors and angiotensin II type I receptor blockers (ARBs) cause an upregulation of ACE2.<sup>2</sup> Patients with hypertension and diabetes are at increased risk of COVID-19 infection.<sup>2</sup> This can possibly be because they are frequently treated with ACE inhibitors and ARBs, which increase the host receptor of the virus.<sup>2</sup>

Carvedilol is a drug with vasodilating properties, initially designed for managing hypertension and coronary artery disease. Unlike ACE inhibitors that increase the expression of ACE 2, carvedilol decreases its expression.<sup>3</sup> This is why, ACE inhibitors or ARBs prescribed for hypertensive patients can be replaced by carvedilol during this pandemic. Moreover, not only patients on ACE inhibitors or ARBs can benefit from carvedilol. Since carvedilol decreases the expression of ACE, which is the COVID-19 host receptor, it can be useful for all COVID-19 patients.

On the other hand, carvedilol can fight COVID-19 by another mechanism. Carvedilol has interleukin 6 (IL-6) suppressing properties.<sup>4</sup> Detectable serum SARS-CoV-2 viral load is closely associated with drastically elevated IL-6 level in critically ill COVID-19 patients.<sup>5</sup> So, carvedilol can be used to target IL-6, which plays a major role in the inflammatory cascade of COVID-19.

In conclusion, we hypothesize that by downregulating ACE and by having anti-IL-6 properties, carvedilol

has the potential to block 2 pathogenic pathways of COVID-19.

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## REFERENCES

1. **Wan Y, Shang J, Graham R, et al.** Receptor recognition by novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS. *J Virol.* 2020;94(7):e00127–20. <https://doi.org/10.1128/JVI.00127-20>.
2. **Fang L, Karakiulakis G, Roth M.** Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? [published correction appears in *Lancet Respir Med.* 2020 Jun;8(6):e54]. *Lancet Respir Med.* 2020;8(4):e21. [https://doi.org/10.1016/S2213-2600\(20\)30116-8](https://doi.org/10.1016/S2213-2600(20)30116-8).
3. **Saijonmaa O, Nyman T, Fyhrquist F.** Carvedilol inhibits basal and stimulated ACE production in human endothelial cells. *J Cardiovasc Pharmacol.* 2004;43(5):616–621. [PMID:15071347].
4. **Kurum T, Tatli E, Yuksel M.** Effects of carvedilol on plasma levels of pro-inflammatory cytokines in patients with ischemic and nonischemic dilated cardiomyopathy. *Tex Heart Inst J.* 2007;34(1):52–59.
5. **Chen X, Zhao B, Qu Y, et al.** Detectable serum SARS-CoV-2 viral load (RNAemia) is closely associated with drastically elevated interleukin 6 (IL-6) level in critically ill COVID-19 patients [e-pub ahead of print]. *Clin Infect Dis.* 2020;ciaa449. <https://doi.org/10.1093/cid/ciaa449>, accessed April 17, 2020.