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## LETTER TO THE EDITOR

## Is photodynamic therapy a viable antiviral weapon against COVID-19 in dentistry?



To the Editor:

We read the recent article<sup>1</sup> that describes a series of 8 cases of oral manifestations of coronavirus disease 2019 (COVID-19) and its management with great interest. In case 1, photobiomodulation was applied as an adjunct for symptomatic relief of oral lesions. We would like to throw light on the viral load reduction of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by photoactivation of the photosensitizer (PS) using a specific wavelength through peroxidation that could expand the scope of photodynamic therapy (PDT) in health care during this pandemic.

SARS-CoV-2 has posed many challenges for health care professionals. The dental fraternity is among the worst-affected sectors during the COVID-19 pandemic. Oral manifestations such as ulcers, blisters, and vesiculobullous lesions<sup>2-4</sup> are often among the earliest manifestations of COVID-19 viral infections, and treatment modalities such as antifungals, topical or systemic corticosteroids, systemic antibiotics, and systemic acyclovir are used to alleviate these symptoms.

However, there are no studies in dentistry to date that report the use of PDT to manage oral manifestations of COVID-19, although it has been used in dental specialties such as periodontics, endodontics, oral medicine, and oral surgery for management of periodontitis, halitosis, intracanal disinfection, oral wound healing, herpes labialis, etc. Previous works<sup>5-7</sup> by the authors of this letter demonstrate the efficacy of PDT in periodontal disease, and it was additionally well tolerated by patients.

Despite PDT's effectiveness against influenza viruses,<sup>8</sup> few studies have proposed the benefits of PDT in lung lesions in COVID-19 cases.<sup>1,9</sup> One of the theories states that photosensitization of viruses induces removal of glycoproteins from the viral surface and the virus thus becomes noninfectious virions, without damage to the membrane.<sup>8</sup> It is interesting to note that PS such as methylene blue (MB), Radachlorin, and 5-amino levulinic acid have shown high antiviral activity against SARS-CoV-2.<sup>10,11</sup> These PS molecules can also act by enticing SARS-CoV-2 virions and attaching to these PS molecules instead of healthy oral tissue<sup>12</sup> or attacking healthy

hemoglobin.<sup>1</sup> Additionally, MB without photoactivation has been found to inactivate SARS-CoV-2 in vitro.<sup>13</sup> This makes MB a strong candidate in the management of COVID-19 lesions. Furthermore, MB has been shown to inhibit the SARS-CoV-2 spike protein's protein-protein interaction and its receptor angiotensin-converting enzyme 2 (ACE-2), a critical step.<sup>14</sup>

The distressful symptoms of oral pain, blisters, and vesiculobullous lesions present in few symptomatic oral lesions in COVID-19-positive patients are attributed to derangement in the ACE-2 receptor and the subsequently increased bradykinin activity as part of the kininogen-kallikrein system.<sup>13</sup> This could also be the reason for the dilation of blood vessels and swelling in these cases. Furthermore, it is speculated that an immunologic phenomenon known as cytokine storm occurs in COVID-19 as in other viral diseases like influenza.<sup>15</sup> This is a crucial finding because the ACE-2 receptor is a known receptor for SARS-CoV-2. These receptors are found in oral mucosa, including the tongue and salivary glands' dorsum, and are responsible for many of the oral lesions in COVID-19-positive patients.

Therefore, based on the available scientific evidence, we propose that PDT is a viable weapon for the prevention and treatment of oral manifestations of COVID-19. In addition to alleviating oral pain and discomfort in symptomatic patients, PDT can be used to disinfect the oral cavity, periodontal pockets, and saliva in asymptomatic patients to manage the outbreak. Further in vitro and clinical studies are needed to unleash the full potential of PDT, which exerts antiviral and antimicrobial effects without the risk of drug resistance and other unwanted side effects.

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### REFERENCES

1. Brandão TB, Gueiros LA, Melo TS, et al. Oral lesions in patients with SARS-CoV-2 infection: could the oral cavity be a target organ? *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2021;131:e45-e51.
2. Iranmanesh B, Amiri R, Zartab H, Aflatoonian M. Oral manifestations of COVID-19 disease: a review article. *Dermatol Ther.* 2020;25:e14578. <https://doi.org/10.1111/dth.14578>. Accessed February 9, 2021.
3. Martín Carreras-Presas C, Amaro Sánchez J, López-Sánchez AF, Jané-Salas E, Somacarrera Pérez ML. Oral vesiculobullous lesions associated with SARS-CoV-2 infection [e-pub ahead of print]. *Oral Dis.* 2021. <https://doi.org/10.1111/odi.13382>. Accessed February 9, 2021.

4. Riad A, Kassem I, Hockova B, Badrah M, Klugar M. Tongue ulcers associated with SARS-CoV-2 infection: a case series [e-pub ahead of print]. *Oral Dis.* 2020. <https://doi.org/10.1111/odi.13635>. Accessed February 9, 2021.
5. Betsy J, Prasanth CS, Baiju KV, Prasanthila J, Subhash N. Efficacy of antimicrobial photodynamic therapy in the management of chronic periodontitis: a randomized controlled clinical trial. *J Clin Periodontol.* 2014;41:573-581.
6. Betsy J, Prasanth CS, Baiju KV, Prasanthila J, Subhash N. Patients' perceptions of antimicrobial photodynamic therapy in the management of chronic periodontitis. *Photodiagnosis Photodyn Ther.* 2016;14:84-90.
7. Joseph B, Janam P, Narayanan S, Anil S. Is antimicrobial photodynamic therapy effective as an adjunct to scaling and root planing in patients with chronic periodontitis? A systematic review. *Biomolecules.* 2017;7:79.
8. Queiroz GB, Foggiato AA, Neto JLT, da Silva DF. Photodynamic therapy and possible action against SARS-CoV-2. *Braz J Dev.* 2020;6:52313-52327.
9. Almeida A, Faustino MAF, Neves MG. Antimicrobial photodynamic therapy in the control of COVID-19. *Antibiotics.* 2020;9:320.
10. Svyatchenko VA, Nikonov SD, Mayorov AP, Gelfond ML, Loktev VB. Antiviral photodynamic therapy: inactivation and inhibition of SARS-CoV-2 in vitro using methylene blue and Radachlorin. *Photodiagnosis Photodyn Ther.* 2021;33:102112. <https://doi.org/10.1016/j.pdpdt.2020.102112>. Accessed February 9, 2021.
11. Sakurai Y, Tun MMN, Kurosaki Y, et al. 5-Amino levulinic acid inhibits SARS-CoV-2 infection in vitro. *Biochemical and Biophysical Research Communications.* 2020.
12. Li W, Moore MJ, Vasileva N, et al. Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. *Nature.* 2003;426:450-454.
13. Ghahestani SM, Shahab E, Karimi S, Madani MH. Methylene blue may have a role in the treatment of corona virus disease of 2019. *Med Hypotheses.* 2020;144:110163.
14. Yang J, Petitjean S, Derclaye S, et al. Molecular interaction and inhibition of SARS-CoV-2 binding to the ACE2 receptor. *Nat Commun.* 2020;11:4541.
15. Liu Q, Y-h Zhou, Yang Z-Q. The cytokine storm of severe influenza and development of immunomodulatory therapy. *Cell Mol Immunol.* 2016;13:3-10.