



EDITORIAL: A New Promising Strategy in the Treatment of COVID-19

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e have recently proposed a new strategy in the treatment of COVID-19; i.e. to make use of antihypoxic agents (1). Based on this hypothesis, we showed (one) mechanism of action dexamethasone as an effective anti-COVID-19 drug in the clinic (2). We proposed other drugs such as Magnesium sulfate (3) or Edaravone (4) and some medicinal plants with high antihypoxic activities such as Crataegus spp. (5), Eryngium caucasicum (6), Sambucus ebulus (7), Allium sativum (8), Juglans regia (9), and Lemon Beebrush (10), or Cantharellus cibarius (11) are good candidates for the treatment of COVID-19.

COVID-19 is currently affecting millions of lives worldwide. Many studies indicate that an elevated level of inflammatory cytokines and pro-inflammatory factors are associated with both increased severity and mortality of the disease. Recently a group of researchers showed using topoisomerase 1 inhibition will suppress the lethal inflammation induced by this virus. The therapeutic efficacy of two doses of Topotecan, an FDA-approved topoisomerase 1 inhibitor, has been reported recently. This drug suppresses infectioninduced inflammation in hamster and mouse models (12). Topotecan treatment for four days after infection reduces morbidity and rescues mortality in animals. These results support the potential of topoisomerase 1 inhibition as an effective therapy against severe SARS-CoV-2 infection. Topotecan

and its derivatives (such as Irinotecan) are inexpensive drugs available most countries. Of course, larger clinical trials are needed to evaluate the efficacy of topoisomerase 1 inhibitors for COVID-19 in humans. Several studies have shown that levels of inflammatory molecules in COVID-19. Increased levels of interleukin-6 and degradation products have been correlated with the risk for death from COVID-19. Therefore, the increased systemic inflammation that occurs during the progression of disease provides a biological rationale for combating hyper-inflammation to reduce the severity of the disease. Therefore, the efficacy of cytokine blockers and anti-inflammatory molecules were tested against COVID-19 (13). But, inhibition of single cytokines such as interleukin 6 or granulocyte-macrophage colony-stimulating factor was not sufficient (14). because many pathways are involved in triggering the inflammatory process. Also, levels of cytokines are the age-dependent and clinical history of patients. It has been previously shown that topoisomerase 1 is required to fully trans activate infection-induced genes and thus controls the inflammatory gene programs during many viral and bacterial infections (15). It has been predicted that this strategy could be useful for future pandemics. Now, based on a newly published paper, topoisomerase 1 inhibitors have the potential for inhibition of COVID-19 infection.

References

- 1. Shamshirian A, Shamshirian D, Hosseinzadeh MH, Ebrahimzadeh MA. A Mini-review and perspective on anti-hypoxic hypothesis of COVID-19. Tabari Biomedical Student Research Journal. 2021;2(4):1-8
- 2. Hosseinzadeh MH, Shamshirian A, Ebrahimzadeh MA. Dexamethasone Vs. COVID-19: An experimental study in line with the preliminary findings of a large trial. Int J Clin Prac. 2020:e13943
- 3. Mohammadi H, Shamshirian A, Eslami S, Shamshirian D, Ebrahimzadeh MA. Magnesium sulfate attenuates lethality and oxidative damage induced by different models of hypoxia in mice. BioMed Res Int. 2020:e2624734
- 4. Shaki F, Mokhtaran M, Shamshirian A, Eslami S, Shamshirian D, Ebrahimzadeh MA. Protective effects of Edaravone against hypoxia-induced lethality in mice. bioRxiv. 2020.
- 5. Ebrahimzadeh MA, Khalili M, Jafari N, Zareh G, Farzin D, Amin G. Antihypoxic activities of Crataegus pentaegyn and Crataegus microphylla fruits-an in vivo assay. Braz. J. Pharm. Sci. 2018;54(2): e17363
- 6. Khalili M, Dehdar T, Hamedi F, Ebrahimzadeh M, Karami M. Antihypoxic activities of Eryngium caucasicum. Eur Rev Med Pharmacol Sci. 2015;19(17):3282-3285.
- 7. Kaveh K, Mohamadyan M, Ebrahimzadeh MA. Antihypoxic activities of Sambucus ebulus leaf and fruit and Myrtus communis leaf in mice. J Mazandaran Uni Med Sci. 2019;29(176):61-73.
- 8. Shahbazee M, Mohammadyan M, Ebrahimzadeh MA. Antihypoxic activities of

- Allium sativum flower in mice. J Mazandaran Uni Med Sci. 2019;29(175):145-149.
- 9. Nabavi SF, Ebrahimzadeh MA, Nabavi SM, Mahmoudi M, Rad SK. Biological activities of Juglans regia flowers. Rev Bras Farmacog. 2011;21(3):465-470.
- 10. Hosseinzadeh MH, Ebrahimzadeh MA. Protective effects of ethanolic extract of Lemon Beebrush (Aloysia citrodora) leaf against hypoxia-induced lethality in mice. Tabari Biomed Student Res J. 2019;1(4):1-7.
- 11. Khalili M, Ebrahimzadeh MA, Omrani F, Karami M. Antihypoxic activities of the golden chanterelle mushroom, *Cantharellus cibarius* (higher Basidiomycetes). International journal of medicinal mushrooms. 2014;16(4): 339-344.
- 12. Ho JS, Mok BW, Campisi L, Jordan T, Yildiz S, Parameswaran S, Wayman JA, Gaudreault NN, Meekins DA, Indran SV, Morozov I. TOP1 inhibition therapy protects against SARS-CoV-2-induced lethal inflamemation. Cell. 2021;184:1-15.
- 13. Merad, M., and Martin, J.C. (2020). Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages. Nat. Rev. Immunol. 20, 355–362.
- 14. Salvarani, C., Dolci, G., Massari, M., Merlo, D.F., Cavuto, S., Savoldi, L., Bruzzi, P., Boni, F., Braglia, L., Turra, C., et al. (2021). Effect of Tocilizumab vs Standard Care on Clinical Worsening in Patients Hospitalized With COVID-19 Pneumonia: A Randomized Clinical Trial. JAMA Intern. Med. 181, 24–31.
- 15. Rialdi A, Campisi L, Zhao N, Lagda AC, Pietzsch C, Ho JS, Martinez-Gil L, Fenouil R, Chen X, Edwards M, Metreveli G. Topoisomerase 1 inhibition suppresses inflammatory genes and protects from death by inflammation. Science. 2016;352(6289).