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## Review: Methylene Blue cheapest Covid-19 Treatment

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### Abstract

Covid-19 contamination normally starts within the breathing tract in which it could reason bilateral pneumonia. The disorder can evolve into acute respiratory syndrome and multi-organ failure; because of viral expand within the blood and an immoderate inflammatory response together with cytokine storm. Antiviral and anti-cytokine tablets have validated to be poorly or in-powerful in preventing disorder progression, and mortality. Persistent efficacy of antiviral tablets might be because of overdue administration, whilst the virus has brought about the inflammatory response and is now not the primary protagonist. We propose in this review article that Methylene Blue could be a therapy option for

Corona Virus Disease in 2019 especially in patients with mild or moderate symptom. We found that methylene blue; a tricyclic phenothiazine compound permitted through the FDA for the remedy of methemoglobinemia and used for different clinical applications inhibits this interaction. It inhibited the access of a SARS-CoV-2 spike bearing pseudovirus into ACE2-expressing cells with comparable IC<sub>50</sub> value. Hence, its antiviral activity in opposition to SARS-CoV-2 may want to make a contribution in making less expensive and broadly to be had drug doubtlessly beneficial within the prevention and remedy of COVID-19 as an oral or inhaled medication.

**Keywords:** Covid-19, SARS-CoV-2, Methylene blue

### Introduction

Coronavirus disease (COVID-19) is a newly found coronavirus that causes an infectious disease.

The majority of patients infected with the COVID-19 virus will have mild to moderate respiratory symptoms and will recover without needing any specific therapy. People, over the age of 65 and those who are underlying with medical conditions such as cardiovascular disease, diabetes, chronic respiratory disease, and cancer, are at a higher risk of developing serious illness.

When an infected individual coughs or sneezes, the COVID-19 virus transmits predominantly through droplets of saliva or discharge from the nose, therefore respiratory etiquette is particularly vital (for example, by coughing into a flexed elbow)

SARSCoV2 primarily infects humans through the respiratory tract, while faecal transmission is possible. In some cases, the infection progresses to acute respiratory distress syndrome (ARDS), a kind of respiratory failure that strikes critically ill individuals quickly.

Multi-organ damage (mostly to the lungs, heart, brain, kidney, liver, and small intestine) and septic or vasoplegic shock are common complications of ARDS. The lungs are the first structures that the virus encounters after entering through the respiratory system, and alveolar epithelial cells abundantly produce ACE2 receptors, which the virus exploits to enter cells.

The virus is able to reach the bloodstream because of widespread alveolar destruction and significant damage to the vascular endothelium. Patients who died of Covid-19 had viraemia and high viral RNA titres in their liver, kidney, and heart.

The blood-brain barrier's ability to inhibit viral entry to the central nervous system remains unknown. However, capillary endothelial cells, a key component of the blood-brain barrier, have a lot of ACE2 receptors and could be a way into the CNS.

Viral infection of the brain via the olfactory system is also a possibility. Endothelial inflammation across vascular beds of multiple organs was found in a series of autoptic Covid-19 instances, which might be explained by the presence of ACE2 receptors on the vascular endothelial cells of all organs. The virus causes an inflammatory response in cells by activating signal transduction pathways, including transcription factor NF-κB, which drive the production of cytokines to prevent viral reproduction and spread.

Could NO and oxidative pressure assume a focal part in expanding hypoxia which would one say one is of the primary confusions in COVID-19 patients? Could this endless loop of NO and ROS be interfered with utilizing a successful what's more, extraordinary enemy of NO and against oxidant treatment?

In medication, methylene blue (MB, the oxidized structure, blue tone), yet not the diminished structure (LMB: Leucomethylene blue, dreary), has been utilized in various illnesses like intestinal sickness, medical procedure, muscular health, bacterial, viral contaminations and whatnot. Regardless of colossal advancement in understanding COVID-19, there is little proof that an answer, remedial or preventive, is near being accomplished. Repurposing of notable, generally accessible medications address an alluring way to deal with accelerate accessibility of dynamic medicines. Such substances as for example hydroxychloroquine and others, are now being scrutinized and in far reaching off name use. For some reasons Methylene blue (MB), the most seasoned manufactured substance in medication (1876 orchestrated by BASF) is a particularly encouraging possibility for a functioning treatment against SARS-CoV-2 contaminated individuals and for COVID-19 patients.

This paper is a part of a work by the research team of Chameli Devi Institute Of Pharmacy. The main objective of this paper is to predict and forecast COVID-19, treatments and recoveries through predictive modelling by the use of methylene blue. At the same time, assess the political and economic impact of the virus spread. We propose a comprehensive framework to manage health information data as a tool for public health practitioners in managing epidemics and crafting public health response and policy. This study focuses on the role of methylene blue as a potent reversible inhibitor of monoamine oxidase A – the enzyme that catalyses serotonin breakdown – and concomitant use with serotonin reuptake inhibitors can inhibit the degradation of serotonin and increase its concentration to toxic levels (serotonin syndrome).

Scigliano, G<sup>(2020)</sup>In this article Giulio Scigliano and team analysed that SARS-CoV-2 infection usually begins within the tract wherever it will cause bilateral respiratory disease. The unwellness will evolve into acute metabolism distress syndrome and multi-organ failure, thanks to infective agent unfold within the blood associate degreed an excessive inflammatory reaction as well as protein storm. Antiviral and anti-cytokine medicine have evidenced to be poorly or ineffective in stopping unwellness progression, and mortality or serious chronic harm is common in severely unwell cases. Further analysis, Giulio said that the low effectivity of antiviral medicine is perhaps thanks to late administration, once the virus has triggered the inflammatory reaction and is not any longer the most protagonist. The comparatively effectivity of opposing protein medicine is explained by the very fact that they act on one or many of the handfuls of cytokines concerned, and since different mediators of inflammation-reactive element and N species-aren't targeted. Once created in excess, reactive species cause intensive cell and tissue harm. For this Giulio recommended that the sole drug glorious to inhibit the excessive production of reactive species and cytokines is methylthionine chloride, an inexpensive dye with antiseptic properties used effectively to treat protozoal infection, tract infections, septic shock, and methaemoglobinaemia. Finally they proposed testing of methylthionine

chloride to distinction Covid related acute metabolism distress syndrome, however significantly they recommend that testing it early in Covid infections to forestall the hyper-inflammatory reaction answerable for the intense complications of the unwellness.

Svyatchenko, V.A<sup>(2020)</sup>Victor and team recently analysed that the COVID-19 pandemic has unfold globally, necessitating the event of latest ways for its bar and treatment. The aim of their study was to gauge the antiviral activity of photodynamic medical aid (PDT) against SARS-CoV-2 in vitro. For this they used the method- Vero E6 cells and SARS-CoV-2 which were isolated in Russia and were used for PDT with stain (MB) and Radahlorin.

They reported that the never-ending optical device with wavelength  $\lambda=662$  nm in doses of sixteen J/cm<sup>2</sup> forty J/cm<sup>2</sup> optical device irradiation was used for PDT of a microorganism suspension and SARS-CoV-2-infected cells. The direct unhealthful result of SARS-CoV-2 was evaluated via lightweight research to calculate the TCID<sub>50</sub> within the samples and perform applied mathematics analysis.

Finally they resulted that the microorganism suspensions of SARS-CoV-2 that had a TCID<sub>50</sub> bigger than 10<sup>3</sup> were inactivated by PDT within the presence of MB and Radahlorin. Vero E6 cells were shielded from 10<sup>4</sup> TCID<sub>50</sub> of SARS-CoV-2 by PDT post infection. The vary of protecting concentrations was one.0–10.0 µg/ml and zero.5–5.0 µg/ml for MB and Radahlorin, severally. In addition, it absolutely was found that MB and Radahlorin conjointly possess vital antiviral activity even while not PDT.

They analysed that the five hundred repressing concentration (IC<sub>50</sub>) against 10<sup>2</sup> TCID<sub>50</sub> of SARS-CoV-2 was found to be zero. The concentrations 22 and 0.33 µg/ml with the addition of MB and Radahlorin, severally, to cells concomitantly with virus, whereas within the case of applying the photosensitizers at three.5 hours post infection, the IC<sub>50</sub> was zero.

Alamdari, D.H<sup>(2020)</sup>Hamidi and team reported that the COVID-19 may be an international harmful event that causes severe acute metabolism syndrome. The mechanism of the sickness remains unclear, and drive is one in every of the most complications. There's no presently approved protocol for treatment. The microbic threat as elicited by COVID-19 causes the activation of macrophages to provide an enormous quantity of inflammatory molecules and gas (NO). Activation of macrophages population into a professional inflammatory composition induces a self-reinforcing cycle. They also said that that Aerophilous stress and NO contribute to the current cycle, established a cascade inflammatory state which will kill the patient. Interrupting this vicious circle by a straightforward remedy might save vital patients' lives. Hamidi analysed that the Nitrite, nitrate (the metabolites of NO), methaemoglobin, and prooxidant-antioxidant-balance levels were measured in twenty five intensive care unit COVID-19 patients and twenty five healthy people. Because the last therapeutic choice, 5 patients were administered methylene radical blue-vitamin C-N-acetyl amino acid (MCN). Nitrite, nitrate, methaemoglobin, and aerophilous stress were multiplied in patients in comparison to healthy people. They said that the four of the 5 patients responded well to treatment. Lastly, NO, methaemoglobin and aerophilous stress might play a central role within the pathologic process of vital COVID-19 sickness. MCN treatment looks to extend the survival rate of those patients. Considering the vicious circle of scavenger cell activation resulting in deadly NO, aerophilous stress, and protein cascade syndrome; the therapeutic impact of MCN looks to be cheap.

Lastly they concluded that a wider trial has been designed. It ought to be noted that the protocol is using the inexpensive

medication that the Food and Drug Administration has approved for different diseases with Trial registration number: NCT04370288.

Hence, we totally agree with their proposal for wider trials for this medication.

Ghahestani, S.M.<sup>(2020)</sup>In this paper, Ghahestani and team raised the theory that Methylene Blue might be a treatment alternative for Covid Sickness of 2019 uniquely when joined with Non Steroid Calming Medications.

They reported that in the past distributions including our own, the part of kininogen framework has been hypothesized. A relationship between's clinical discoveries of the sickness and this component has been attracted to mean a crucial job of kininogen-kallikrein framework in pathophysiology of the infection. In that the conceivable part of Icatibant, Ecallantide and Aprotinin in the treatment of this infection has been raised.

Over here they have underscore on a significant post-receptor component of bradykinin that is Nitric Oxide. Finally, Ghahestani resulted that in these present circumstances point since we discovered how admittance to these novel treatment chosen people might be costly and excessively expensive. Therefore we are zeroing in on conceivable part of an old yet "secretive" drug in particular Methylene Blue. This prescription may cut short impacts of Bradykinin by hindrance of Nitric Oxide synthase inhibitor and advance oxygen immersion while it is cheap and pervasively available. Clinical examinations can't be over accentuated.

### Summary and discussion

In conclusion methylene blue can be prove to be an effective and inexpensive alternate medicine for the treatment of covid- 19 disease in patients with mild to moderated symptoms. It can also be used intravenously in patients with severe symptoms. But we suggest to take it as oral dosage form as it is easy administer and inexpensive. This paper is a part of a work by the research team of Chameli Devi Institute of Pharmacy. The main objective of this paper is to predict and forecast COVID-19, treatments and recoveries through predictive modelling by the use of methylene blue. Hence, its antiviral activity in opposition to SARS-CoV-2 may want to make a contribution in making less expensive and broadly to be had drug doubtlessly beneficial within the prevention and remedy of COVID-19 as an oral or inhaled medication. Moreover, in future we are going to do the survey of the cases treated with methylene blue targeting a particular city and also the molecular docking studies of methylene blue for COVID-19.

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