

Mini Review

Coronavirus and pH

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Summary

This article investigates the viability of SARS-CoV-2 and its dependence on pH levels, specifically focusing on the difference between the pH stability intervals for the coronavirus and human blood. Human blood typically maintains a pH range of around 7.35 to 7.45, while SARS-CoV-2 exhibits stability within the pH range of 6.0 to 6.5. The study aims to elucidate the critical role of hemoglobin in maintaining pH balance and explores its implications for viral susceptibility. The findings emphasize the importance of reinforcing the alkalinity of the medium as a means to weaken the virus. The research contributes to the understanding of pH-dependent mechanisms in viral infections and provides valuable insights for the development of potential therapeutic strategies.

Introduction

The COVID-19 (SARS-CoV-2) pandemic continues to pose significant challenges worldwide, with the number of cases and deaths reaching alarming levels. As of 7 May 2023, the cumulative number of confirmed cases has exceeded 765 million, with over 6.9 million deaths reported globally [1].

In this critical time, the entire world, regardless of its level of development, is fervently seeking solutions to combat the challenges posed by COVID-19. The number of deaths due to the virus has already reached several million within a span of more than 3 years, with no end in sight. It is in the context of these dire circumstances that we focus our attention.

The global community, encompassing both highly developed and less developed nations, is fervently pursuing an intense search for solutions to address the challenges posed by the COVID-19 pandemic [2,3].

To this day, numerous approaches to the treatment of COVID-19 have been devised and are extensively employed. Numerous studies and real-world evidence demonstrate that vaccines are an effective tool in combating the disease. They provide significant protection against severe disease, hospitalizations, and deaths associated with COVID-19 [4]. However, in the terminal stage of the disease when the body is in a critical condition, vaccination may have limited impact on the illness. Vaccines are typically intended to prevent disease or reduce its severity, but they may not always provide complete protection or treatment in later stages of the

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disease [5]. It is also important to note that the effectiveness of vaccines may be diminished in certain population groups, especially in individuals with weakened immune systems or underlying health conditions [6].

Mechanical Ventilation Devices (MVDs) become offer hope, especially for individuals in high-risk areas who are severely affected by the virus. At first, glance, connecting patients to MVDs and providing supplemental oxygen should aid in saving lives, particularly when the lungs fail to function at the terminal stage. However, the statistics surrounding MVDs are relatively unknown [7]. Also, it plays a crucial role in supporting lung function in patients with respiratory insufficiency. Delivering controlled amounts of air and oxygen helps maintain proper oxygenation and removal of carbon dioxide from the lungs. However, prolonged and inappropriate use of mechanical ventilation can have adverse effects on lung mechanics, potentially leading to ventilator-induced lung injury and impairing overall lung function [8].

This method serves as a reminder of the crucial functional role performed by the lungs in the process of oxygenating the blood. While inhalation and exhalation are vital auxiliary functions, the primary function of the lungs is to maintain oxygenation. Upon infection with the coronavirus, this critical function is compromised, leading to its impairment [9]. Lung tissue atrophy may contribute to this severe syndrome,

although it is not exclusive to cases of severe lung damage. Notably, even in the absence of severe lung damage, a significant reduction in blood oxygenation (oxygen saturation) occurs, despite adequate partial pressure of gaseous oxygen ($P(O_2)$ in the lungs [10,11].

At the same time, the significance of tissue acidity-alkalinity roles in the human body, particularly in blood oxygenation, has not been adequately acknowledged. This article can serve as a foundation for further experimental research and the development of treatment recommendations for COVID-19, especially during its critical stages.

Blood oxygenation and pH

Significantly, the level of blood oxygenation is intricately linked to another essential parameter known as the hydrogen ion concentration (pH). Let us recall that pH is defined as $-\log CH^+$, where CH^+ represents the concentration of hydrogen ions in moles per liter (mol/L). In a neutral medium, such as distilled and purified water devoid of carbon dioxide, the pH is 7.00 at a temperature of 298K. In an acidic environment, the pH decreases towards 0, whereas in an alkaline medium, it rises towards 14. In a healthy human body, the blood pH is maintained at around 7.35 to 7.45 [11]. Acidosis is observed when the pH drops below normal, while alkalosis occurs when the pH rises above normal levels. Even a slight deviation of pH by 0.3 can lead to nervous system depression, and at a pH of 7.11 or lower, it can result in fatality. For other organs and tissues, broader pH ranges are acceptable, such as pH levels of 7.0-7.5 for saliva, and noticeably lower than 7.0 for urine and gastric juice. The blood's pH stability is upheld through a system of three buffer solutions: carbonate, phosphate, and primarily, hemoglobin [12]. Therefore, in addition to its primary role in oxygen transportation to tissues and removal of carbon dioxide, hemoglobin (Hb) also contributes to maintaining the blood's optimal pH level.

Let us now examine the chemical processes schematically. When hemoglobin interacts with oxygen, it undergoes a transformation into oxyhemoglobin:



On the other hand, as a base, hemoglobin reacts with H^+ ions.



Hence, a competition between reactions (1) and (2) arises, involving the interaction of O_2 molecules and H^+ ions with a hemoglobin molecule. An important consequence emerges from this interplay: as the partial pressure of oxygen decreases in the external environment (i.e., the lungs) and the pH of the medium (i.e., blood) decreases, the binding of O_2 to hemoglobin weakens, leading to impaired blood oxygenation. This phenomenon is known as the Werigo-Bohr effect, well-established in physiology [13,14]. Let us now consider the

fate of oxyhemoglobin. Upon reaching the tissue cell, it must release the O_2 molecule and simultaneously acquire the CO_2 molecule, which is produced during the oxidation of glucose ($C_6H_{12}O_6$). In a high partial pressure of CO_2 within the cell, the CO_2 molecule displaces the O_2 molecule from oxy-hemoglobin, resulting in the formation of carbo-hemoglobin, following the scheme:



This process is facilitated by H^+ ions, which counteract the binding of CO_2 molecules to water molecules. In the alveoli of the lungs, under conditions of high partial pressure of oxygen and low partial pressure of carbon dioxide, the reverse process occurs, where CO_2 is displaced from carbo-hemoglobin and replaced by O_2 [15].

However, what about the coronavirus?

As is widely known, the coronavirus exhibits a distinctive morphology, resembling a "ball with horns," and has a size ranging from approximately 100 nm to 120 nm, making it nearly a nanoparticle. In addition to proteinaceous protrusions, the virus particle contains a coiled molecule of ribonucleic acid (RNA) enveloped by a protective lipid membrane. The virus possesses specific pH stability limits, ranging from 6.0 to 6.5 [16], which are likely influenced by the following factors:

- The inherent acidic properties of RNA, primarily due to the prevalence of acidic phosphorus-containing groups over basic nitrogenous bases.
- The lipid membrane's heightened resistance to hydrolysis in an acidic environment compared to an alkaline one [17]. Notably, the virus's resistance substantially diminishes as the pH falls below 6.0 or exceeds 6.5 [18,19]. It is determined that the virus exhibits maximum stability at 4 °C [20].

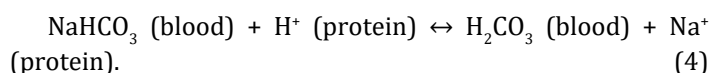
From these observations, the following conclusions can be drawn:

- The pH stability ranges of the virus and the human blood differ fundamentally.
- When the virus infiltrates the bloodstream, it either perishes or adjusts the blood's pH to its own stability range, at least on a localized scale. In scenario (b), where there is insufficient overall immunity and a compromised blood pH regulatory system, the body faces inevitable demise. The exact mechanisms by which the virus achieves its deceitful pH adaptation, with varying degrees of success, remain uncertain [21,22]. One plausible scheme is as follows: initially, the virus disrupts gas exchange in the lungs, damaging the alveoli responsible for the diffusion of O_2 molecules into the blood and the removal of CO_2 . This disruption leads to the inevitable acidification of the blood, aligning its pH

with the virus's preferred range, thereby establishing a favorable environment for the virus to thrive [23]. The attenuation of reaction (1) and intensification of reaction (2) impairs the function of hemoglobin in O₂ transport to the tissues, resulting in tissue hypoxia and acidification due to CO₂ accumulation [24]. Consequently, the viral infection's shockwave spreads much faster than the virus itself. This proposed scheme helps elucidate the underlying causes of the explosive and often tragic course of the disease [25]. Revising this manuscript enhances our understanding of the coronavirus's interplay with pH dynamics, highlighting its impact on disease progression. The insights gained from this research can guide the development of targeted therapeutic strategies aimed at mitigating the virus's devastating effects.

Blood pressure and pH

Under the influence of various factors, including those caused by a coronavirus, a malfunction of the buffer systems occurs, namely, H⁺ ions in the protein walls of blood vessels are replaced by Na⁺ ions. The latter is built into the walls of blood vessels, which swell as a result of enhanced adsorption of water (Na⁺·nH₂O), and, having only one outlet, narrow the lumen of blood vessels. At the same time, H⁺ ions enter the bloodstream and provide a pH shift towards lower values, i.e.:



The phenomenon of acidosis occurs, i.e., there is a correlation between a decrease in pH and an increase in blood pressure. In the future, lowering the pH itself results in disturbances in the functioning of the body systems. Specifically, it sends a signal to the central nervous system, leading to vasodilation in the blood vessels (there is a possibility for the brain which tissue is soft), resulting in an increase in intracranial pressure. Therefore, reports of a positive effect of hypertension medications on the course of the disease infected with coronavirus are of interest [26]. On the other hand, it is not surprising that coronavirus causes or exacerbates hypertension, and its presence in the patient is a risk factor (along with diabetes, age, etc.) [27].

If gas acidosis appears (impaired gas exchange in the lungs, blood, and tissues), the addition of NaCl to food leads to the following effects: Na⁺ ions entering the blood are exchanged to H⁺ of proteins on the walls of blood vessels (see above); Cl⁻ ions are partially absorbed by red blood cells, but mainly remain in the bloodstream, forming the strong acid HCl with the H⁺ ions. This causes (or intensifies) sharp acidification (acidosis) with all the resulting physiological consequences [28,29].

What should be done?

Undoubtedly, the foremost priority is to create unfavorable conditions for the virus by slightly alkalizing the medium

while maintaining strict and continuous pH control to ensure optimal levels [30]. This crucial step sets the stage for the implementation of various medical treatment methods in a controlled manner. The challenging task at hand, both now and in the foreseeable future, lies in ensuring and sustaining the appropriate blood pH level.

However, amidst the tremendous stress brought about by the pandemic, the solution encompasses three key aspects:

- a) Urgent measures involve the cautious use of micro-additives with distinct alkaline properties in the inhaled air. These additives should be administered carefully to mitigate potential risks and facilitate therapeutic efficacy.
- b) Midline, using ordinary slaked lime to absorb CO₂ from the area where the resuscitation patient with COVID-19 is located (in indirect contact): the fact is that a decrease in the level of CO₂ to 1/5 of the usual content in the atmosphere is equivalent to an increase of the partial pressure of oxygen from 0.2 Bar in the atmosphere to 1 Bar in the patient's mask (lime is sometimes used in medical procedures, for example, to neutralize acidity in the stomach or as an antiseptic component in toothpaste and mouthwashes [31,32]; also lime is used to regulate soil pH and improves conditions for plant growth and increase crop yield).

This is associated with the consumption of a significant amount of scarce oxygen, primarily in liquid form. Therefore, the proposed approach not only yields therapeutic effects but also conserves a significant amount of scarce resources, particularly for countries located within hot climate zones.

- a) Long-term perspectives involve the development of theoretical foundations and extensive practical testing to establish daily monitoring and correction of blood pH as a strategic line of defense against current and future infectious diseases, encompassing both viral and bacterial pathogens.

Conclusion

The findings underscore the need to reinforce the alkalinity of the medium as a means to weaken the virus. Understanding the pH-dependent mechanisms in viral infections contributes to the development of potential therapeutic strategies. By alkalizing the medium, carefully monitoring pH levels and exploring innovative approaches, we can pave the way for effective treatment strategies against current and future infectious diseases.

Furthermore, the article discusses the correlation between blood pressure and pH levels. Malfunctioning buffer systems and acidosis can lead to an increase in blood pressure. The presence of the coronavirus exacerbates hypertension, making it a risk factor for severe illness.

To address these challenges, urgent measures involving the cautious use of micro-additives with alkaline properties in the inhaled air are recommended. Additionally, the use of slaked lime to absorb CO₂ in the vicinity of COVID-19 patients can help conserve oxygen resources. Long-term perspectives include the development of strategies for daily monitoring and correction of blood pH as a strategic line of defense against infectious diseases.

In summary, by understanding the interplay between pH dynamics, viral infection, and disease progression, we can develop targeted therapeutic strategies and pave the way for a healthier future. Implementing measures to alkalize the medium and closely monitor pH levels is crucial in combating the challenges posed by infectious diseases such as COVID-19.

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