Hypotheses: implementation of Le Chatelier’s principle as a potential integrative method to prevent and or cure coronavirus

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\textbf{Abstract:} The COVID-19 is an infectious disease caused by a newly discovered coronavirus (SARS-CoV-2) and is mainly considered a respiratory tract illness, even though it may influence other body functions. The virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes. The number of infected people and deaths associated with COVID-19 is increasing on a daily basis and the current third wave of the pandemic appears to be worse than the one that swept several countries over the summer. The only aspect that can be reasonably managed in this pandemic is the environmental stress, which is important to boost the patient's immune system and the patient's ability to recover. Here we propose a potential integrative method to prevent and or attempting to cure coronavirus patients using safe and available resources that can be administered easily by most patients. This treatment is taking advantage of the equilibrium Law as explained by Le Chatelier principle and implemented through the use of antiseptics/disinfectants that can be administered by inhalation without harming the patient's health. This proposed method is expected to reduce the COVID-19 virus load to a threshold that could boost the patient's immune system and speed recovery.

\textbf{Keywords:} COVID-19; SARS-CoV-2; environment stress; disinfectant; concentration gradients; bicarbonate

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\section*{Introduction}

The number of people infected with the new coronavirus continues to increase; by mid-December 2020, there were approximately 75 million people infected and 1.6 million death worldwide. Health management, control, and/or treatment of COVID-19 coronavirus disease is limited (1). Classically, the general method of inactivating viruses is either through macromolecules such as vaccines, which have the potential to block receptors and ultimately block the viral activity or through micromolecules, where the RNA sequence could be selectively targeted and block processes essential for viral replication. Fortunately, two vaccines have been approved, short term safety is promising, but long-term safety remain an open question (2). Vaccine for COVID-19 is prophylactic, taken for prevention not for cure. For this reason, COVID-19 treatment must be investigated and implemented quickly to contain the global spread of the virus and make it easily available worldwide.
One option was well evaluated, based on the treatment of the symptoms associated with the viral infection. For this reason, hydroxychloroquine (3) and remdesivir (4) were introduced as potential drugs to cope with the viral symptoms. Both drugs will neither cure the coronavirus nor limit its spread, but the two drugs and others could potentially contribute to a more tolerable progression of the virus. Currently, there is a consensus among scientists that the best available option is still to activate the patient’s immune system. The response of the immune system varies according to age, state of health, and environmental stress. In a pandemic situation, age and patient’s health cannot be managed, while environmental stress can be manipulated more effectively to stimulate the immune response. Patients infected with coronaviruses are under great mental and physical stress, therefore it is necessary to create favorable circumstances that can cope with the environmental stress (5). Mental stress can be managed by specialists, whereas physical stress, which is the most important, can only be managed by physical means.

In this context, we propose a new hypothesis, based on the principle of Le Chatelier to reduce the coronaviruses to a threshold that could boost the immune system (6) and allow the patient to better cope with the infection. The method could conceivably be used as an adjunct therapy, with potential to be effective, environmentally friendly, easily accessible, and convenient to protect patients from coronaviruses and most likely from other viral infections.

**Hypothesis**

In general, the dose determines the toxicity. In the case of coronavirus, this means that when the infectious dose is increased, the probability of infection and illness is likely to increase. For this reason, wearing a mask is recommended. When an infected person moves without a mask, the virus particles begin to move in the same direction, with relatively few microscopic states. As the intensity increases, the potential energy of the virus increases, initiating a coordinated action of particles that cause the virus to turn into aggressive particles that can infect and spread infection to others. While the mask dispersing virus particles lead to a non-concerted action, the movement of particles became uncoordinated, random in all directions, with many microscopic states. The increasing disorder of the virus particles, resulting from dispersion and subsequent dilution of the particles in the atmosphere, reduces their potential and makes the virus less effective (7).

It is generally believed that reducing the infectious dose of COVID-19 could reduce its infectious potential and lead to less severe cases (8). The high infectious dose is associated with a higher viral load and thus higher disease progression and transmission. The virus spreads from person to person primarily through saliva droplets or discharge from the nose when an infected person coughs or sneezes. The risk of infection is likely to be significant only if a minimal infectious dose is developed or viral loads reach thresholds for transmission (9). This concept led us to propose a new hypothesis based on a dose-dependent response and dispersion attitude, in which an individual with a high infectious dose is likely to develop severe COVID-19 symptoms and transmit infection to others. Droplet transmission requires close contact between susceptible and infectious individuals, and the more a virus has replicated in the body, as a consequence, the higher the viral load, which in turn is likely to be a strong determinant of transmission risk. This perspective led us to propose that the intensity of coronaviruses in the patient’s body (inside) and in the patient’s surroundings (outside) is at a constant ratio. As the intensity of the virus within the infected person increases, the intensity around the infected person likewise increases. Similarly, when the intensity inside decreases, the intensity outside decreases. We therefore propose that if the intensity of the virus outside is decreased, the intensity inside will decrease accordingly (10). The hypothesis is based on the principle of Le Chatelier (11).

The principle of Le Chatelier represents self-organization in nature, as it defines the direction in which the system will move to cope with the change of system conditions. When a system in equilibrium is subjected to changes caused by factors such as concentration, temperature, or pressure, the system tends to shift its equilibrium position to counteract the effect of the disturbances without changing the equilibrium constant. Consider a beaker filled with water, at a certain temperature, pressure, and concentration, the liquid water is in equilibrium with the water vapor that forms above the surface of the liquid. The rate of condensation (vapor to liquid) is equal to the rate of evaporation (liquid to vapor); *Figure 1A*. When a stress is applied to the system that allows some of the water vapor to be removed, then, according to Le Chatelier’s principle, the rate of evaporation exceeds the rate of condensation (*Figure 1B*) and more liquid water is transformed into vapor until equilibrium is restored (*Figure 1C*), thereby reducing the volume of liquid and water vapor simultaneously (12). For this reason, the evaporation of water is accelerated by
increasing the temperature or reducing the vapor pressure by means of an air fan or rotary evaporator.

Human being is a very important biological system, complex but responsive to different states; strong, weak, happy, angry, young, old, healthy, sick. The intensity of these states is strongly influenced by changes in ion concentration, potential energy, entropy, longevity, and diffusion. These processes exist in the biological system and play an important role in determining the direction and the intensity of the state. The non-biological system tends towards equilibrium, whereas biological system tends towards homeostasis (13). Le Chatelier’s principle can be adapted to the biological system and might be used to cope with diseases and maintain a compatible and homeostasis system.

In the case of coronavirus infection, we postulate that the intensity (concentration) of coronaviruses in the patient's body (inside) and in the patient's surroundings (outside) is at a constant ratio (Figure 2). Assuming that the intensity of the coronaviruses in the patient’s surroundings (outside) would decrease as a result of a stress disorder, it can be predicted according to Le Chatelier’s principle that sneezing and coughing would shift the balance from the inside to the outside and thereby reduce the intensity of the coronaviruses in the patient’s body. Sneezing, coughing and tears are produced to fight infections and the average number of particles exhaled per cough and sneeze is $5 \times 10^3$ and $1 \times 10^6$, respectively (14). The movement of the viruses from the inside, to the outside, is continued until equilibrium is restored. The observation is supported by the theory of concentration gradients; substances move from a high concentration area with high potential

Figure 1 The implementation of the Le Chatelier principle for the evaporation of water. (A) Liquid water and water vapor are in equilibrium, with the condensation and evaporation rates being equal; (B) when water vapor is exposed to a stress, such as an air fan, the vapor is moved away from the surface and the vapor concentration is reduced; at this point the evaporation process is accelerated to counteract the stress; (C) the stress is removed and the equilibrium is restored.

Figure 2 Implementation of Le Chatelier’s principle as a potential therapy for the coronavirus. (A) The intensity of the viruses inside and outside is in equilibrium; (B) the movement of the viruses from the inside, I, to the outside, II, is increased as a result of external stress (humidifier); (C) enough of I moves to II, so that the equilibrium is restored.
Experimental observations show that alcohols increase the disinfecting effect and can inactivate the coronavirus within a short time. Alcohols are known disinfectants that are toxic when inhaled and could worsen the patient's health. Most of the present antiseptics/disinfectants are used on inanimate objects and surfaces. Antiseptics are applied either to the skin or mucous membranes; in the case of pulmonary disease, inhalation therapy can be applied. Most antiseptics/disinfectants have the potential to inactivate viruses, thereby reducing the viral load in the environment. As disinfection progresses, the equilibrium and movement of viruses from the inside of patient's body to the outside continues to shift until the equilibrium is restored. The intensity of the viruses from inside and outside reaches an equilibrium threshold of inactivation, stress is reduced, potential energy is restored, and the immune system is boosted more effectively.

**Rationalization of the disinfectant**

In practice, disinfection effectively reduces the risk of disease transmission and propagation to an acceptable threshold. For more effective implementation of the hypothesis, a specific set is required to increase the entropic state and reduce the virus intensity around the patient. The rational selection of the therapeutic method is crucial to ensure that the virus can be inactivated without harming the patient's health. The most suitable means to reduce the virus intensity around the patient are antiseptics/disinfectants. Antiseptics are used to eliminate microorganisms and/or inactivate viruses on living tissue whereas disinfectants are used on inanimate objects and surfaces. Antiseptics are applied either to the skin or mucous membranes; in the case of pulmonary disease, inhalation therapy can be applied. Most antiseptics/disinfectants have the potential to inactivate viruses, thereby reducing the viral load in the environment. As disinfection progresses, the equilibrium and movement of viruses from the inside of patient's body to the outside continues to shift until the equilibrium is restored. The intensity of the viruses from inside and outside reaches an equilibrium threshold of inactivation, stress is reduced, potential energy is restored, and the immune system is boosted more effectively.

**Proposed treatment and delivery way of bicarbonate mixture**

Based on the above information, the target buffer should contain 5% sodium ions with pH close to 7.4, which is identical to the blood's pH. Sodium chloride and acetic acid is added to adjust the pH of the bicarbonate to match the body pH and form a buffer system with high capacity. The sodium ions are small, diffuse easily into the atmosphere, and are likely to create a region with a high ionic concentration gradient. Five percent sodium ion is derived from 2% sodium chloride and 3% of sodium bicarbonate, sodium ions from sodium chloride act as a common ion effect, and according to the Le Chatelier principle, the reverse reaction [Equation 3: Eq. 3] accelerates in an attempt to reduce the effect of the added sodium ion. As a result, the equilibrium position shifts to the left, slightly lowering the pH from 8.2 to 8.02 and suppressing the formation of the more basic solution, sodium carbonate, which could be produced from the bicarbonate and carbonate equilibrium.

The proposed treatment consists of a mixture of 3% sodium bicarbonate and 2% sodium chloride (pH =8.02).
To the mixture, 3% vinegar (vinegar contains 5% acetic acid and 3% vinegar is equivalent to 0.025 M acetic acid) and 1% flower extract such as rose water or mint fragrance are added to speed up the movement of ions in a refreshing atmosphere (Figure 3). The final mixture has a pH of 7.4 with high buffering capacity. It is interesting to note that bicarbonate-buffer therapy can be administered by inhalation or, if necessary, by spraying into each nostril. Best suited to choose the inhalation method as primary bicarbonate prevention/therapy for COVID-19 coronavirus and other serious viral infectious diseases. The inhalation method can be easily performed at home by inhaling the vapor from an electric humidifier that contains the treatment mixture. The movement of vapor generated by the humidifier disperses the virus particles, increasing their entropic state and reducing their potential for infection and transmission. The humidifier and the mixture can be found in practically every household and is affordable for people, primarily in developing countries (25,26).

Though the mechanisms of virus inactivation by chemicals are poorly understood, initial reactions of viruses with disinfectants lead to breaches of the lipid bilayer. In the case of the sodium chloride-bicarbonate mixture, ionized particles such as Na$^+$, Cl$^-$, HCO$_3^-$ saturate the surrounding atmosphere and attract viruses electrostatically via a membrane protein amino acid residue, preferably building blocks with electrically charged side chains. The high ion concentration produces a high osmotic effect, potentially leading to an increase in liquid density, which is associated with water removal from the virus. When the ion concentration is increased, the strength of the electric field accelerates the flow of ions, which in turn increases the collision of the ions with the viruses and eventually leads to an exponential decrease up to a threshold where the virus is inactivated, however, it is unknown how much damage must be done to the viruses before a virus infection can be prevented (27). Since the fusion of the virus with the target cell membrane is enhanced at low pH, the mixture of sodium chloride, bicarbonate and acetic acid is an ideal buffer solution that is compatible with the human body and contributes to maintaining the homeostatic pH.

**Conclusions**

During the last 20 years, three novel human coronaviruses emerged, and probably more viruses will appear. COVID-19 coronavirus continues to spread and infect more people every day. Even though several available drugs and new vaccine reported to have different degrees of success, still COVID-19 officially has no cure and third wave has already started in certain countries. Viruses have a high mutational propensity that reduces vaccine efficacy, thereby non-specific, non-selective viral inactivation is considered more effective. Antiseptics/disinfectants have the potential to inactivate the virus non-specific non-selective. The proposed method has high potential for preventing and/or treating coronavirus patients and could be effective for the treatment of other viral infections as well. Treatment has no limitations in terms of mutation, availability and cost. It is readily available at most households and is cost-effective for people worldwide to obtain and use. We believe patients infected with COVID-19 should be allowed to apply this treatment and the treatment should be publicly made available to them. The same method can be applied for effective disinfection and prevention of the disease.

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Footnote

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jphe-20-132). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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