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Review Article

Role of Materials on Prevention of Viral Transmission: A Review

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Abstract

COVID-19 pandemic has intensified anxiety globally about the predominance of practicing the conventional rules to prevent the widespread use of microorganisms. Engineering research and investigation regarding this issue to design a surface including texture that prevents or kills microbe's adherence has revived. It is revealed that there are many research studies available on antibacterial coatings or materials. However, inadequate information exists regarding the use of antiviral materials for prevention of transmission. Although, due to the emergence of new viruses, new materials are added to the literature through experimentation and/or hypothesis. The mixture of antiviral and antibacterial chemical entities may be a key player in terms of preventing disease. In this review, the discussion of the importance of corona-virus, how it affects humans, and the predominant antiviral and antibacterial materials of various classes such as copper, TiO2, and silver have been discussed. The material's surface defense mechanisms against pathogen colonies are addressed in-depth, highlighting crucial differences that will decide the parameters and guide the future production of advanced antibacterial and/or antiviral materials. Authors also proposes an effective composite material as surface coating for spreading of virus that include corona virus.

Keywords: Corona-Virus; SARS-CoV-2; Covid-19; Antiviral Materials; Antimicrobial Materials

Introduction

It is properly not known; how long coronaviruses will survive on various material surfaces. However, a stipulated amount of survival time has been estimated or postulated for some materials. Droplets and/or aerosol generated by infected people are supposed to be the most common mode of transmission. It is reported that the coronavirus enters at the mouth or nose region, when people usually rub them with the carrier, and goes down deeper into the body. It ends up in the lungs, the spleen, or the intestines. The immune system is there to protect our body. It is postulated that coronavirus affects some of our immune cells also. This creates a big confusion among the immune cells, whether to attack the infected cell or the healthy cell. Corona infects the immune cells and causes them to overreact and excites them with a bigger problem. In a way, it puts the immune cells into a kind of fighting match and sends much more immune cells than it should [1]. This results in more damage and wastage of cells. Two types of cells, in particular, cause the greatest damage. First, neutrophils, which kill everything, including our cells. As they arrive in huge numbers, they start destroying friends as well as enemies by pumping out enzymes. The other important kind of cells that go into the battlefield is the dangerous T-cells, which usually make infected cells commit controlled suicide as they are also confused and start ordering the healthy cells to kill themselves too. In most cases, the immune system gradually regains control. It kills the infected cells, identifies the viruses that are trying to infect new cells, and cleans up the battlefield (lungs). If it's a critical case, the protective lining of the lungs will perish and millions of epithelial cells will have died. Bacteria also infect the alveoli (small airbags through which breathing occurs), thus making it tougher to breathe. SARS-CoV-2 (Corona-virus) structure is a spherical shell or a hull around the Genetic material containing DNA and RNA. They also have proteins that are shown as protruding spikes around the surface [1,2].

Nanotechnology based treatment is considered one of the critical treatments for infectious diseases caused by viruses and bacteria, both predicted and unforeseen. Antimicrobial agents, generally, are chemical compounds that are either natural or synthesized polymer embedded without or with nanoparticles. Antiviral properties of nanoparticles, in particular, have been well established, and due to their large surface area to volume ratio, they display a significant response even at low concentrations. Their main purpose is to act as an antimicrobial agent, inhibiting or killing pathogenic microbes such as viruses, fungi, and bacteria.

The main objective of the current article is to study about the role of free radical, Reactive Oxygen species (ROS) and photocatalytic properties on the viral growth. Based on the effectiveness of these parameters on viral growth, the study aims to recommend antiviral surfaces or materials in the health care facility in the current and future scenario.

Copper

It is reported that the antimicrobial properties of copper are due to its ionic nature. When a foreign organism, such as a bacterium or virus, comes into contact with copper or one of its alloys, the virus recognizes copper ions as an essential nutrient and starts to consume them. The ionic dose becomes lethal as more and more copper ions penetrate the viral cell [3,4]. The influx of ions destabilizes the cell's electrical micro-current, recognized as the transmembrane potential, and essentially short-circuits the viral membrane, making these amounts of copper toxic to the viral cell. This compromises the membrane's integrity, allowing more copper ions to enter the cell. This has a major impact on the cell's ability to metabolize and, as a result, kills it by destroying its DNA and RNA. The list of microbes it can destroy is truly amazing, including coronavirus, norovirus, E. coli, MRSA, and certain antibiotic-resistant infection strains. There are three mechanisms has been postulated by which copper surfaces affect microbes or viruses. i) Membrane Depolarization, ii) ROS generation, iii) Contact Killing. It can be inferred that copper in the form of native copper is more effective as compared to alloy. Brass may be more effective than bronze. The different established mechanism and hypothesis has been discussed below.

Membrane depolarization

Membrane Depolarization is the most commonly proposed mechanism that is for copper to act as an antibacterial and antiviral agent by killing the microbes. Generally, there is a potential difference of 100-200 milli-volt between the outside and the inside of the cell. This difference is induced by the cell membrane. The inner membrane has less negative potential. This potential difference is reduced by the copper ions by binding to the bacterial or viral cells which are charged negatively in both inner and outer cell membranes giving rise to membrane depolarization as shown in the Figure 1. This causes a rupture or a leak in the membrane when the potential difference between the two membranes becomes zero [3-5]. This mechanism is widely found in the gram-negative and gram-positive bacteria where copper ions are bound to carboxylic groups, and peptidoglycans.

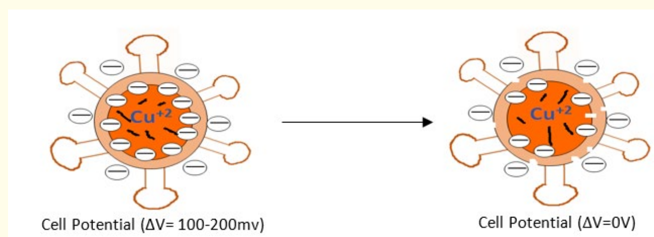

Figure 1: Diagrammatical representation of the Membrane depolarization.

ROS based hypothesis and antimicrobial mechanism

Although there are various antimicrobial materials and different mechanisms to tackle different viruses, there are some common features among nanoparticles that are to be addressed. One common feature is that there is an interaction of ROS such as superoxide (•O_2–), hydrogen peroxide (H_2O_2), and hydroxyl radicals (•OH) with the virus. As a result, the DNA or RNA inside the virus is ruptured. First, let us look at how these reactive oxygen species are formed. During mitochondrial electron transport [6], the majority of reactive oxygen species are generated as by-products.

Furthermore, ROS are produced as required intermediates in metal-catalyzed oxidation reactions as shown below. 2 unpaired electrons lie in different shells in the outer electron shell of atomic oxygen. Oxygen is vulnerable to formation of radicals due to its electronic structure. Hydroxyl ion, Hydroxyl radicals, Hydrogen peroxide, Superoxide, and nitric oxide are the ROS in general. These are synthesized by adding electrons which thereby causes a sequential reduction. The formation of the ROS in metal-catalyzed oxidation reaction is shown in following sequential reactions.

$$Cu^{+2} + H_2O_2 \rightarrow Cu^{+} + \bullet O_2^{-} + 2H^{+} \text{---------(1)}$$

$$Cu^{+} + H_2O_2 \rightarrow Cu^{+2} + \bullet OH + OH^{-} \text{-------(2)}$$

$$Cu^{+} + O_2 \leftrightarrow Cu^{+2} + \bullet O_2^{-} \text{------(3)}$$

One of the most commonly used markers of free radical development, which is a measure or a marker of oxidative stress, is lipid peroxidation. Free radicals also attack unsaturated fatty acids, which are generally found in cellular membranes [7]. In certain reactions, a hydrogen moiety is captured by a free radical in order to generate unsaturated carbon which eventually forms water in a chain reaction. This results in a fatty acid unpaired electron, allowing it to capture oxygen and form a peroxyl radical. Carbonyl compounds such as MDA are formed due to the instability of lipid peroxides. This involves a chain of reactions and finally forming malondialdehyde. This oxidative stress further ruptures DNA and RNA inside the cell and eventually, the cell dies. ROS prevent the viral growth on the surface by damaging the cellular membrane, disrupting the respiratory system and inhibiting the network signal of the viruses. Schematic representation of the ROS generation and its application in prevention of viral growth has been shown in the Figure 2.

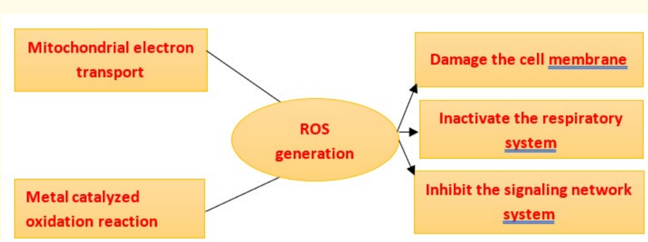

Figure 2: Schematic representation of the ROS based antimicrobial properties.

Contact killing

Metallic copper or alloyed Copper surfaces are well known for a mechanism called contact killing under non-wet as well as moist/wet condition [8-11]. Direct hand contact on the surface is related to the non-wet condition whereas sneezing and coughing resembles the application of microbes through wet condition. Killing kinetic of microbes on the non-wet surface is relatively high due to the liquid surface between the microbes and surface which protects the microbes [12]. Copper has a free electron in its outer orbital shell which enable the copper to take part in oxidation-reduction reactions easily. This is the reason, rapid dissolution of copper ion from copper surface takes place. These ions blast the pathogen like an onslaught of missiles, preventing cell respiration and punching holes in the cell membrane or viral coating and creating free radicals that accelerate the kill, especially on dry surfaces. Most importantly, the ions seek and destroy the DNA [9] and RNA [13] inside a bacteria or virus, preventing the mutations. Figure 3 shows the stepwise the possible series of events during the contact killing by the metallic copper/alloyed copper surface.

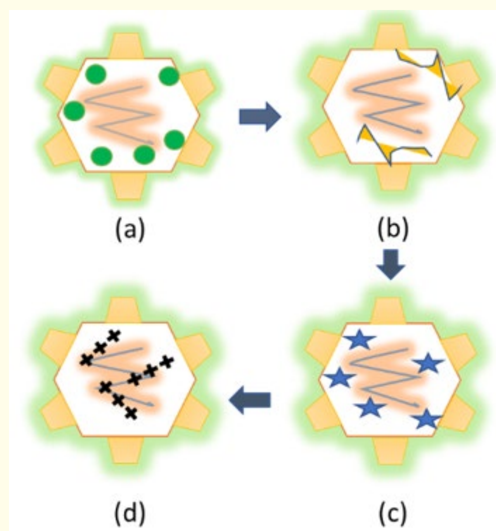

Figure 3: Stepwise possible series of events during the contact killing on copper surface (a) dissolution of copper ions from copper surface causing cell damage (b) Cell membrane ruptures due to copper ions (c) Copper induce the formation of free radicals (ROS) (d) RNA and DNA destroyed by ROS subsequently degrades genomic materials which prevents mutations of virus.

TiO2

TiO2 Nano-particles have photocatalytic properties, which controls the microbial growth as shown in some study [14,15]. These photocatalytic properties enable the excitation of electron from the valance bond to conduction band under the enough UV exposure and generates the electron-hole pair. This is the reason TiO_2 has a wide bandgap of 3.2eV. These hole-electron pairs react in various ways on the surface and generate the ROS such as $O_2^{\bullet-}$ and OH• radicals. Photogenerated ROS attacks by different mechanisms to microorganisms (virus/fungi/bacteria). On one track, the cell membrane can be damaged, while on another, it can react to and disrupt the cell wall [16]. Some researchers also found that the signaling system and the respiratory system of the virus have been inactivated [8,16]. Application of TiO_2 Surface as antiviral surface with regard to interaction nature with bacteria/virus surfaces due to its nano-scopic characteristics. TiO_2 nanoparticles change surface-area-to-volume ratios to maximize ROS interaction. whereas the cell membrane and wall rupture by intracellular oxidative damage is supplemented by the small size of nanoparticles.

Silver

Ag and its oxide (Ag_2O) Nanoparticles are also used in healing of wounds, engineering of tissues, food packaging, water disinfection, and dentistry. According to various studies, during the interaction between microorganisms and Ag nanoparticles, Ag+ ions interfere with the cell wall peptidoglycan of bacteria, causing structural variation, which contributes to increased membrane permeability and cell death. By combining with proteins of bacteria via available sulfhydryl groups, Ag nanomaterials often help to prevent DNA replication.

DNA replication capacity is lost as a result of destructive interaction with bacterial DNA and Ag_2O. Ag nanoparticles have been shown to have a substantially stronger antiviral response to HIV-1 (98%) than Au nanoparticles (6–20%). As a result, we can see that Ag is a valuable and promising antimicrobial solution for a variety of microbes, and the process with resultant antimicrobial activity varies depending on the Ag-based content.

Hypothetical material

It has been established that ROS plays an important role to fight against viral transmission. Furthermore, free electron is having some role in that mechanism. Research indicates that high conductor like copper as semiconductor in the form of quantum dot are effective to prevent transmission and treatment. Considering predominate role of free electron and photocatalytic effect of Cu and TiO2 respectively authors recommend Cu-TiO2 nanocomposites as a material of choice to prevent transmission of COVID-19 virus. It will generate free electron and/or ROS and affect virus growth considering virus as also charged particle. Some research on the Cu deposited TiO2 thin films [17] and Cu-TiO2 nanofibers [18] on the surface under visible light with weak UV illumination (1 $\mu W/cm^2$) which corresponds to UV intensity of indoor light in general has been done. Research suggests Photocatalytic process causes the partial decomposition of the outer cell membrane while copper ions penetrate into cytoplasmic membrane resulting in complete loss cell's integrity [17]. Although, study has been done on E. coli and bacteriophage f2 strain rather than corona virus. Cu-TiO2 films or nanocomposites also possesses the deodorizing and self-cleaning properties besides its antiviral properties. One more important consideration regarding the usage of Cu-TiO2 nanocomposites are its properties such as density and Hardness. Density decreases and hardness increases with increasing the TiO2 particle [19]. Thus, these outstanding properties of the Cu-TiO2 nanocomposites are best suited to being used in present and future at health care facility considering the current scenario of COVID-19 Pandemic in order to prevent virus infection. Although, its proper efficacy against COVID-19 virus is still unknown and investigation are immediately needed to be started in this regard.

Will coating of copper at health care facility will be beneficial: Data based study

In India, the prevalence of hospital-acquired infections is 14.7 percent, which means that approximately 15 people out of every 100 are affected by the hospital climate. And nearly every 37 in 1000 people are hospitalized in India with over a quarter of the older population [20]. This means that installing copper in hospitals could prevent tens of thousands of infections per year. Increasing the use of copper in our public spaces and hospitals will be a step backward, as copper was previously used much more commonly. Handrails, doorknobs, elevator keys, public benches, and many more frequently touched surfaces can be replaced or coated with copper.

The major reason is due to the high upfront costs [21], hospitals are hesitant to use copper and take this life-saving measure.

Copper was phased out of hospitals in the first place. It's due to our own vanity and an affinity for other materials like plastics, stainless steel, and aluminum. Copper door knobs, railings, and beds were replaced with other similar materials.

According to US statistics, installing copper on just 10% of a hospital's highest-risk surfaces costs about $50,000. The costs are much higher in India because of the amount scaling to the hospitals. The theory is that looking at costs in this manner is a bad idea. The total cost of healthcare-acquired infections on an annual basis is truly staggering. In the United States, about 99000 people die each year as a result of health-care-associated infections, with treatment costs totaling nearly 35 billion dollars. This suggests that the total cost of treating a hospital-acquired infection is nearly $30000 [4]. This number rises much higher in India, where the population and infection rate are both higher [20]. However, it was discovered that installing copper to only 10% of the surfaces in one hospital over a year resulted in over 15 fewer infections. Even if we use the lowest cost for treating a healthcare-acquired infection, the savings from the copper installation are almost $400,000 (savings of over 13 times). With these figures, it's fair to say that if the copper percentage was raised above 10%, the savings will be much greater, and most importantly, more patient lives would be saved [4]. Small changes such as copper door handles and copper bed frames, for example, have been shown to measurably reduce the rates of healthcare-acquired infections in hospital environments. Although copper, like all other elements, is a finite resource, it is unlikely that we will run out of it anytime soon. According to the International Copper Association (ICA), the world's copper reserves are currently at 830 million tonnes. According to our current use, this supply should last around 50 years. But copper, practically, is one of the most recycled products on the planet, so we'll be able to use it for a long time. Also, even though copper oxidizes and turns green, it retains its antimicrobial properties. Another problem is that households generally don't find copper attractive, it loses its coloration over time but never loses its antimicrobial property. Although, the world is in crisis, and people should not be thinking in the direction of attractiveness, rather think in the direction of safety.

Authors suggest the use of very thin nano copper coating to take care of cost. Nano copper is having better surface properties and may be better kinetics with reference to generation of ROS. Further, the contact killing mechanism will be effective on that surface. TiO2 nano-coating may be tried also considering photocatalytic properties.

Conclusion

Considering the above review, Authors have found that using the Copper, TiO2 and Ag2O nanoparticles in public places, most touched surfaces and health care facility prevent the risk of infection from the microbes. Considering the properties of the Cu and TiO2 nanoparticles against the microbes, Authors also recommend the hypothetical Cu-TiO2 nanocomposites to be considered for research and investigation against COVID-19 to combine the effect of Cu and TiO2 particles in order to tackle the current pandemic as well as for future applications.

Conflict of Interest

All authors listed declares that they have no conflict of interest.

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