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Review

Disinfectants against SARS-CoV-2: A Review

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Abstract: The pandemic due to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has emerged as a serious global public health issue. Besides the high transmission rate from individual to individual, indirect transmission from inanimate objects or surfaces poses a more significant threat. Since the start of the outbreak, the importance of respiratory protection, social distancing, and chemical disinfection to prevent the spread of the virus has been the prime focus for infection control. Health regulatory organizations have produced guidelines for the formulation and application of chemical disinfectants to manufacturing industries and the public. On the other hand, extensive literature on the virucidal efficacy testing of microbicides for SARS-CoV-2 has been published over the past year and a half. This review summarizes the studies on the most common chemical disinfectants and their virucidal efficacy against SARS-CoV-2, including the type and concentration of the chemical disinfectant, the formulation, the presence of excipients, the exposure time, and other critical factors that determine the effectiveness of chemical disinfectants. In this review, we also critically appraise these disinfectants and conduct a discussion on the role they can play in the COVID-19 pandemic.

Keywords: SARS-CoV-2; disinfectant; virucidal activity; alcohol; quaternary ammonium salt; chlorine-releasing agents; chlorine dioxide; hydrogen peroxide and peracetic acid; iodophor; ozone

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1. Introduction

Since the first outbreak at the end of 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is still raging around the world, bringing about detrimental effects to the world economy and society [1–3]. As of May 2022, there have been over 515 million confirmed cases of COVID-19, including more than 6 million deaths, reported by the World Health Organization (WHO) [4]. Current studies suggest that the SARS-CoV-2 virus can spread from an infected person's mouth or nose in small liquid particles when they breathe, sneeze, cough, or speak [5]. It may also be transmitted via contact by touching contaminated surfaces, followed by touching the mouth, nose, or eyes. Experimental studies have shown that SARS-CoV-2 can survive on various plastic, latex, glass, and metal surfaces for hours to days [6]. Additionally, epidemiological evidence from the field suggests that the virus can survive on the outer packaging of cold-chain foods kept in a low-temperature environment and has been proven to maintain infectivity [7,8]. Therefore, the fomite transmission of SARS-CoV-2 is certainly plausible [9].

A highly effective treatment for this emerging infectious disease is lacking to date, although several drugs and vaccines have been found to improve clinical outcomes in large trials, and the rapid development and production of vaccines has permitted large-scale vaccination in many countries [10–12]. However, vaccine development still faces challenges, even with novel platforms [13]. More evidence is required before we know exactly how effective these drugs and vaccines are, especially when new virus variants constantly emerge [14,15]. These challenges become even greater due to the virus's high transmissibility rate and long incubation period, as was evident with the Omicron variant [3]. In this context, preventive measures such as rapid detection, the isolation of cases, and the early quarantining of close contacts of positive cases, as well as mask use, physical distancing,

8.2. Peracetic Acid

Peroxyacetic acid is considered a more potent biocide than hydrogen peroxide against a broad spectrum of pathogens at lower concentrations (<0.3%) [105]; thus, it is frequently recommended for disinfecting medical devices [17]. However, higher concentrations of peracetic acid (>100 ppm) may be necessary to reduce non-enveloped viruses on surfaces, foods, and fomites [106].

Peroxyacetic acid also decomposes to safe by-products (acetic acid and oxygen) and has the added advantages of being free from decomposition by peroxidases, in contrast to hydrogen peroxide, and remaining active in the presence of organic loads. As with hydrogen peroxide, vapor-phase peroxyacetic acid is also more active (as oxidants) at lower concentrations than in the liquid form. Its main application is as a low-temperature liquid sterilant for medical devices, flexible scopes, etc., and is also used as an environmental surface sterilant [36]. Its main advantages over other vapor-phase systems include low toxicity, rapid action, and good activity at lower temperatures.

Similar to hydrogen peroxide, peroxyacetic acid probably denatures proteins and enzymes and increases cell wall permeability by disrupting sulfhydryl (-SH) and sulfur (S-S) bonds [36]. Finnegan et al. published an in vitro study on the action of hydrogen peroxide and peroxyacetic acid on proteins under physiological conditions. They found that peroxyacetic acid, in particular, oxidizes amino acids efficiently, degrades bovine serum albumin, and reduces the efficiency of the enzyme alkaline phosphatase at millimolar concentrations. These multiple targets imply that microbial organisms are less likely to mobilize resistance [99]. Additionally, there was an apparently large number of free radicals that arose from the reactions of the peroxide with organic compounds, and free radicals are highly reactive; peroxyacetic acid probably inhibits or kills microorganisms using several mechanisms, though the exact mechanism is still controversial due to the complexity of the reaction pathway [107].

Ansaldi et al. reported the effectiveness of peroxyacetic acid on coronaviruses: a 0.035% (35 ppm) solution inhibited SARS-CoV replication in a cell culture with a contact time of <2 min, while the same concentration did not affect the viral genome after 30 min of exposure [105]. Another study suggested that SARS-CoV can be inactivated with 500 to 1000 ppm of peroxyacetic acid [108]. A recent study showed similar results; the effective inactivation of SARS-CoV-2 after an exposure time of 60 s in carrier tests was documented by more than 4.0 $\log_{10}$ [28]. This study found that peroxyacetic acid could inactivate SARS-CoV-2 (4 $\log_{10}$ reductions) in 5 min in an ethanol bath at −20 °C, but could not completely destroy the RNA of SARS-CoV-2 after 3 h of exposure [58].

9. Iodophor

Iodophor is a complex of iodine and a solubilizing agent or carrier because iodine alone is not stable in water. This formation allows the sustained release of iodine and has powerful microbicidal activity [109]. The most commonly used iodophor is povidone iodine because of its rapid, broad-spectrum antimicrobial activity, even at low concentrations, and due to its established safety profile [110,111].

It is free molecular iodine that mediates the antimicrobial activity of iodophor. Iodine rapidly penetrates into microorganisms and reacts with key groups of proteins (in particular, the free sulfur amino acids cysteine and methionine leading to the loss of protein disulfide linkages) [17,81]. The iodination of phenolic and imidazole groups of the amino acids tyrosine and histidine and pyrimidine derivatives of cytosine and uracil lead to steric hindrances in hydrogen bonds and the denaturation of DNA. Iodine binding to unsaturated fatty acids has been shown to alter the physical properties of lipids and lipid-containing membranes which culminate in cell death [112].

As one of the important medicines on the WHO List of Essential Medicines, povidone-iodine (polyvinylpyrrolidone iodine, PVP-I) is routinely used in surgical procedures, including the disinfection of skin when formulated into scrubs or handwashes and for oral cavities through oral sprays and mouth rinses [113–115]. The combination of PVP-I with