

The Application of Non-chloride Based Disinfectants in Inactivation of SARS-CoV-2 in Personal Protective Equipment, Air and Surfaces of Hospitals

Hastanelerdeki Kişisel Koruyucu Donanımlarda, Havada ve Yüzeylerde SARS-CoV-2'nin İnaktivasyonunda Klorür Esaslı Olmayan Dezenfektanların Uygulanması

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Abstract

As Severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2) emerged in 2019, scientists sought to find a way of inactivating this new virus to effectively disinfect surfaces, air, hands, etc. The first proposed manners were on the basis of chemical disinfectants such as chlorine and bleach, however, application of these methods can result in some hazards for human beings and the environment. Therefore, new methods such as ultraviolet (UV) radiation were recommended. Not only these new methods can accelerate the inactivation of SARS-CoV-2 in a more efficient way, their hazards and side effects are also less when compared to chlorine-based disinfectants. In this review, we discussed the utilization of UV-C, hydrogen peroxide, ozone, and cold plasma as new, nonthermal methods to disinfect personal protective equipment, air, and surfaces in hospitals, since hospitals were one of the major sources of Coronavirus disease-2019 infection and members of health care team were highly prone to being infected.

Keywords: COVID-19, disinfectants, hospital infections, pandemic, SARS-CoV-2 inactivation

Öz

2019'da Şiddetli akut solunum sendromu-Koronavirüs-2'nin (CoV-2) ortaya çıkması ile bilim adamları yüzeyleri, havayı, elleri vb. etkili bir şekilde dezenfekte etmek için bu yeni virüsü etkisiz hale getirmenin bir yolunu bulmaya çalıştılar. Önerilen ilk yöntemler, klor ve ağartıcı gibi kimyasal dezenfektanlara dayanıyordu, ancak bu yöntemlerin uygulanması insan ve çevre için bazı riskler taşıyordu. Bu nedenle ultraviyole (UV) radyasyon gibi yeni yöntemler önerildi. Şiddetli akut solunum sendromu-CoV-2'nin etkisiz hale getirilmesini daha verimli bir şekilde hızlandıran bu yeni yöntemler, klor bazlı dezenfektanlara kıyasla daha az risk taşımaktadır ve daha az yan etkiye sahiptir. Bu derlemede, hastaneler Koronavirüs hastalığı-2019 enfeksiyonunun ana kaynaklarından biri olduğundan ve sağlık ekibinin üyeleri enfekte olmaya oldukça yatkın oldukları için hastanelerde kişisel koruyucu donanımları, havayı ve yüzeyleri dezenfekte etmek için yeni, termal olmayan yöntemler olarak UV-C, hidrojen peroksit, ozon ve soğuk plazmanın kullanımını tartıştık.

Anahtar Kelimeler: COVID-19, dezenfektanlar, hastane enfeksiyonları, pandemi, SARS-CoV-2 inaktivasyonu

Introduction

In December 2019, a group of people started to arrive at Wuhan's hospitals with severe pneumonia of unknown etiology.

This was reported to the World Health Organization (WHO), and on January 7, 2020, a new coronavirus was found among these patients, which was officially called Severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2)^[1]. This new virus causes

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a disease called Coronavirus disease-2019 (COVID-19), which has nosocomial transmission capacity^[2,3].

Till now, a definitive cure for COVID-19 is not been achieved, thus people try to apply preventive strategies, such as isolating infected people, obeying the social distancing rules, using personal protective equipment (PPE), and applying effective disinfection methods^[4-7].

However, the application of these methods faces difficulties. During the current pandemic, a global shortage of PPE has been experienced, and the WHO recognizes that the current global stockpile has been inadequate, especially for surgical masks and filtering facepiece respirators (FFRs)^[8]. Disinfecting and reusing PPE (particularly FFRs) can be an effective way to deal with the unprecedented PPE shortage^[9,10].

In addition to the use of PPE, disinfection of surfaces is very necessary to prevent SARS-CoV-2 transmission^[11]. Therefore, chloride-based disinfectants are commonly used in hospitals to disinfect surfaces. However, thorough manual surface cleaning may be insufficient to completely diminish pathogens or viral transmission^[12]. Moreover, chlorine-based disinfectants can have harmful effects on the human respiratory system^[13] and may damage the ecology and environment^[14]. Therefore, new alternative methods with higher efficacy should be applied^[12].

This study aimed to investigate the efficiency of new approaches against SARS-CoV-2. These alternative methods are usually more efficient (in disinfecting this virus) than the common methods and do not possess the risks and side effects of chloride-based disinfectants^[12,15].

SARS-CoV-2 Stability on Different Surfaces and Its Surrogates

Recent studies showed that SARS-CoV-2 has different stabilities on different surfaces (Table 1). The SARS coronavirus maintains its stability and viability on smooth surfaces in normal air conditions (temperature of 22-25 °C and relative humidity of 40-50%) for over 5 days. However, viral stability remarkably diminishes (>3 log reduction) at higher relative humidity and temperature (e.g., 8 °C and 95%, respectively)^[16]. It clarifies why some tropical Asian countries (Malaysia, Thailand, and Indonesia) with elevated temperatures and high humidity have not experienced severe SARS outbreaks in their populations^[16].

Researching SARS-CoV-2 may be highly dangerous since scientists are at risk of infection and the use of surrogate coronaviruses can cross these hurdles^[17]. Bacteriophages represent strong surrogates for airborne virus research, and specific precautions for biocontainment are not required, as they are riskless for humankind^[18,19].

Bacteriophage's diversities are high on both genetic and morphological levels, which provide a large pool of pathogens, wherein some phages share structural similarities with eukaryotic viruses^[20]. Furthermore, double-stranded DNA genome-tailed phages (Caudovirales) seem to be the most studied of all bacterial viruses and can be used in a wide range of applications that involve aerosol investigations (Figure 1)^[21]. The following surrogates were used (for literature studies) to evaluate the effectiveness of disinfectants against coronaviruses based on biophysical properties and genomic structures: Human coronavirus 229 E, murine hepatitis virus, transmissible gastroenteritis virus, and feline infectious peritonitis virus^[22].

Ultraviolet

Based on the purpose of this study, ultraviolet (UV) light is classified into three different groups of wavelength as follows: UVA (320-400 nm), UVB (280-320 nm), and UVC (200-280 nm)^[23]. UVC light has much greater germicidal characteristics than both UVA and UVB since UVC photons can be sensitively absorbed by the intercellular constituent of pathogens (like

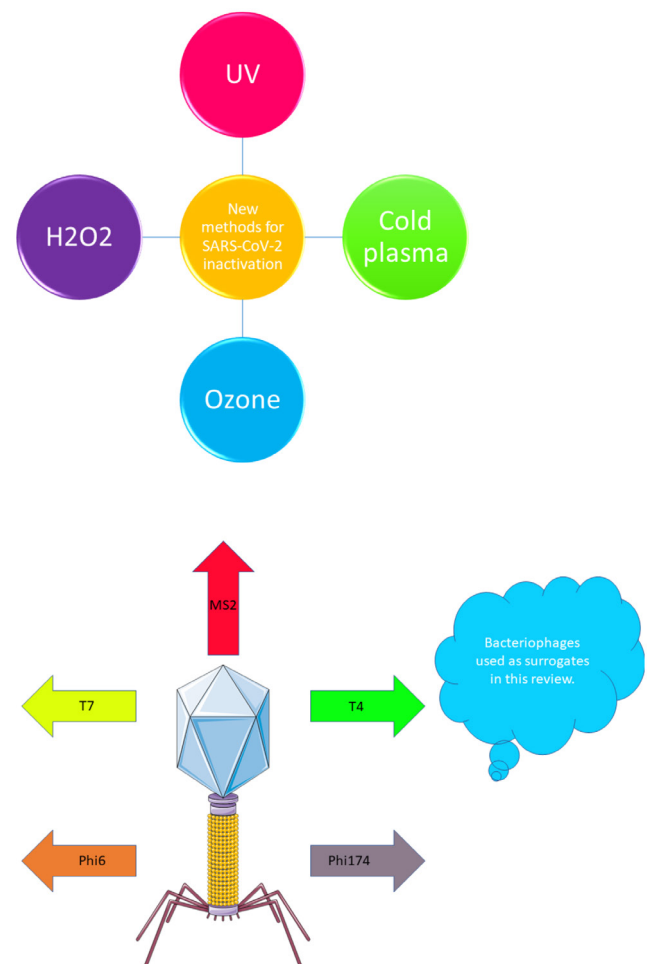


Figure 1. The bacteriophages which can be surrogates of Severe acute respiratory syndrome-Coronavirus-2

RNA, DNA, and proteins) and it disables viruses to replicate (Table 2)^[10,24].

Moreover, research findings prove that UV is a reliable virucidal technique. Tseng and Li^[25] tested the effectiveness of UV against viruses, which were on the surface of gelatin made medium (Table 3), and evaluated the susceptibility of four different viruses according to their genome. They revealed that UV is a reliable and effective method to disinfect surfaces.

Several studies have examined the effectiveness of UV in microorganism inactivation on the PPE. A study evaluated the influence of pulsed xenon ultraviolet (PX-UV) cleaning on an Ebola-surrogate virus on crystal containers and PPE content to explore its possible benefits in PPE decontamination^[26]. This study aimed to decrease the pathogen loading before doffing. They discovered that PX-UV exposure significantly reduced the viral load of glass containers and PPE.

However, the efficacy of UV radiation is dependent on the dose or fluence and shadowing, as it solely inactivates by the irradiation of media^[27], and high doses of UV can cause changes in the penetration and resistance of PPE^[28].

Ozone

Ozone is a potent oxidizing agent that is widely used in the pharmaceutical and food industries, as well as in the environmental regulation of pathogenic microorganisms (Table 4)^[29-31]. Compared with the chlorine-based disinfectants, ozone is 25 times more powerful than Hypo chloric acid and 2,500-3,000 times more effective than hypochlorite (OCI-)^[32]. Furthermore, ozone gas production is easier, more economical, and safer to handle and apply^[33]. Additionally, ozone molecules can easily decompose back to oxygen, thus the environmental hazards may be decreased^[34].

There are currently no investigations that explicitly evaluate ozone's disinfection method against SARS-CoV-2. However, Tizaoui^[35] believe that ozone would attack the spike proteins and lipid envelope of SARS-CoV-2, which would therefore inhibit its capability to bind to cell receptors and replicate in cells.

Additionally, the use of pseudoviruses (as a model for testing coronavirus) at different ozone concentrations has been studied. Exposure of these viruses to ozone for 20 min at 1000 ppm, 30 min at 100 ppm, and approximately 40 min at 30 ppm decreased the viral infection by 95%. These results suggest that even at

Table 1. The stability of SARS virus on different surfaces^[61]

Type of surface	Type of SARS corona virus	Temperature	Persistence
Metal	Genetic variant P9	Room temperature	5 days
Wood	Genetic variant P9	Room temperature	4 days
Paper	Genetic variant P9	Room temperature	4-5 days
Paper	Genetic variant GVU6109	Room temperature	24 hours to <5 min
Glass	Genetic variant P9	Room temperature	4 days
Plastic	Genetic variant HKU39849	22-25 °C	≤5 days
Plastic	Genetic variant P9	Room temperature	4 days
Plastic	Genetic variant FFM1	Room temperature	6-9 days
Disposable gown	Genetic variant GVU6109	Room temperature	2 days to 1 hour

SARS: Severe acute respiratory syndrome

Table 2. The sensitivity of different coronaviruses to UVC^[62]

Virus	Irradiation wavelength (nm)	Log reduction dose (mJ/cm ²)	Sample condition
HCoV-229E	222	0.56	Aerosol
MHV	254	0.66	Aerosol
MERS COV	254	Successful inactivation	Droplets
TGEV	254	3.68	Liquid (with 10% blood platelet concentrate)
SARS-CoV-1	254	4.6	Aliquots of virus
SARS-CoV-2	260-285	≥4	Stainless steel
CCoV L-71	254	10.55	Liquid (thin layer of cell culture with fetal bovine serum)

HCoV-229E: Human corona virus, MHV: Murine coronavirus, TGEV: Transmissible gastroenteritis virus, MERS: Middle east coronavirus, SARS-CoV: Severe acute respiratory syndrome coronavirus, CCoV: Canine coronavirus

low ozone exposure, ozone is an effective disinfectant for the enveloped pseudoviruses^[36].

Ozone can be utilized as a sanitizer/disinfectant in both aqueous and gaseous forms in several industrial and home settings. Ozone is more reactive in its gaseous form; however, aqueous ozone disinfection is advantageous. Thus, controlling the oxidant concentration of ozone in liquid form is easier^[29,37]. Additionally, despite the complications associated with breathing ozone in a gaseous state, aqueous ozone does not affect human skin cells since its cell destruction effect is specific to microbial cells^[38]. Finally, ozonated water shows limited cytotoxicity to human keratinocytes as experimentally compared with different hand disinfectants^[39].

Moreover, ozone can be used to inactivate microorganisms on the surfaces of PPE and enable its reuse (Figure 2)^[40]. Furthermore, exposure to the suggested dose of ozone does not change the efficiency of N95 filtering materials^[40]. Subsequent tests showed no loss of filtration efficiency or mechanical properties for either substance when exposed to 20 ppm ozone for up to 36 h, thus corresponding to 7230 minutes disinfection cycles at 20 ppm^[41].

Cold Plasma

The fourth state of matter is plasma. It is a partially or completely ionized gas where the outer-shell electrons are stripped of the atoms and/or molecules^[42]. Among the plasma's various constituents, UV radiation and reactive oxygen and/or nitrogen molecules have the most essential antimicrobial capabilities^[43]. Production of ROS and RNS leads to the breakage of C-C, C-O, and C-N bonds of microorganisms^[44]. The level of these reactive species can be modified by plasma source design, operating conditions, feeding gas types, and the microorganism itself^[45]. Plasma can be roughly classified into thermal (or equilibrium plasma) and nonthermal [nonequilibrium or cold plasma (CP)]. The CP method can be used at room temperature and thus is ideal for the different biological materials, including solids, aerosols, and liquids^[46].

In replacing traditional disinfectant methods for the inactivation of viruses, CP has shown great promise^[47]. Wu et al.^[48] evaluated the efficacy of atmospheric pressure CP (APCP) against the MS2 virus and revealed that the MS2 virus survival levels (for the airborne states) were significantly reduced by APCP exposure. Additionally, >95% (1.3 log reduction) of the viruses, which were in the air, were inactivated by the APCP

Table 3. The inactivation of different viruses by UV irradiation^[63]

Virus genome type	Amount of inactivation	The required dose of UV (mJ/cm ²)
ssRNA	90%	1.32-3.20
	99%	2.51-6.5
ssDNA	90%	2.5-4.47
	99%	5.04-8.34
dsRNA	90%	3.80-5.36
	99%	7.75-10. 57
dsDNA	90%	7.70-8.13
	99%	15.54-16.20

ssRNA: Single-stranded RNA, dsRNA: Double-strand RNA, ssDNA: Single-stranded DNA, dsDNA: Double-stranded DNA, the RH (relative humidity) is 55%, UV: Ultraviolet

Table 4. The effectiveness of ozone molecule in inactivation of some aerosol viruses^[64]

Name of virus	Genome	Size (nm)	Envelop	RH value	Inactivation	Ozone concentration (ppm)
MS2	ssRNA	25	NO	55%	90%	3.43
					99%	6.63
Phi X174	ssDNA	25-27	NO	55%	90%	1.87
					99%	3.84
Phi 6	dsDNA	75-86	YES	55%	90%	1.16
					99%	2.5
T7	dsDNA	45	NO	55%	90%	5.20
					99%	10.33

The contact time in this experiment was 13.8 seconds.

ssRNA: Single-stranded RNA, ssDNA: Single-stranded DNA, dsRNA: Double-stranded RNA, dsDNA: Double-stranded DNA, RH: Relative humid

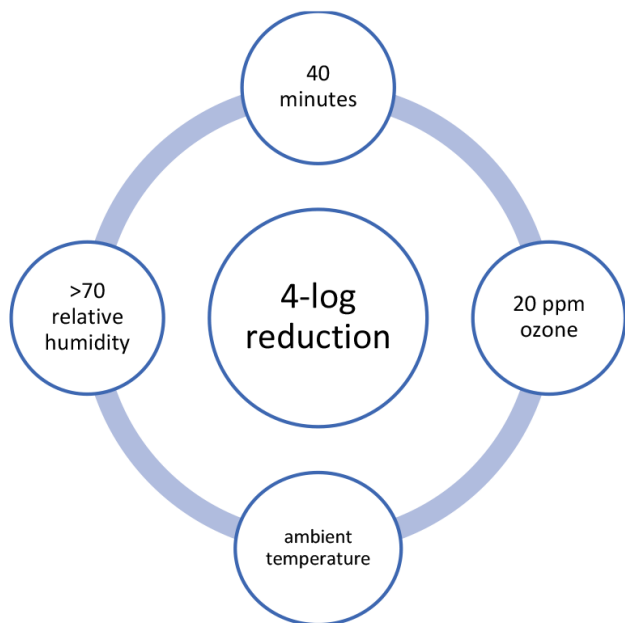


Figure 2. Condition needed to inactivate Severe acute respiratory syndrome–Coronavirus-2 on personal protective equipments and surfaces using ozone

application (utilization of ambient air as the gas transporter) at 28 Watts for approximately 0.12 seconds. Furthermore, influenza A and B viruses and respiratory syncytial virus (RSV) have been treated with the pulsed high-voltage CP source^[49,50] and revealed that CP treatment can completely inactivate the RSV on the surface of the glass after 5 min of exposure^[49]. Lastly, treatment with Ar-fed cold atmospheric

plasma (CAP) has been proven to rapidly and effectively disable SARS-CoV-2 on a wide variety of surfaces (including plastic, metal, and cardboard) that people regularly touch^[51]. Therefore, CAP can be a confident and efficient way to avoid viral transmission and infection.

Hydrogen Peroxide (H₂O₂)

H₂O₂ is a powerful and potent oxidant, which works against different microorganisms (such as viruses and bacteria) by the formation of HO (Figure 3)^[52,53]. It is used for preserving, disinfecting, and sterilizing applications in both liquid and gas types. The H₂O₂ gas method has become a common alternative to the other physical and chemical-based antimicrobial techniques because of its low temperature, rapid efficacy, limited toxicity concerns, and compatibility with surface materials^[54].

Two different commercial vaporized H₂O₂ generation systems are offered to decontaminate microbiological laboratories. The first one is H₂O₂ vapor (HPV) and the second one is vapor H₂O₂ (VHP). The HPV approach infuses HPV at a low level into the enclosures, thus small condensation occurs on the inside surface. VHP, on the other hand, works as a dry device, lowering the humidity levels inside the enclosures and preventing condensation on surfaces^[55]. The Environmental Protection Agency registers both condensing and non-condensing systems and both are effective against bacterial spores and other microorganisms^[56-58].

Saini et al.^[59] studied the efficacy of H₂O₂ in decontamination of different PPE, including face shields, coveralls, and N95 masks. Three biological markers, namely *Mycobacterium smegmatis*, *Escherichia coli*, and *Bacillus stearothermophilus* spores, are regarded as the gold standard for inactivation processes,

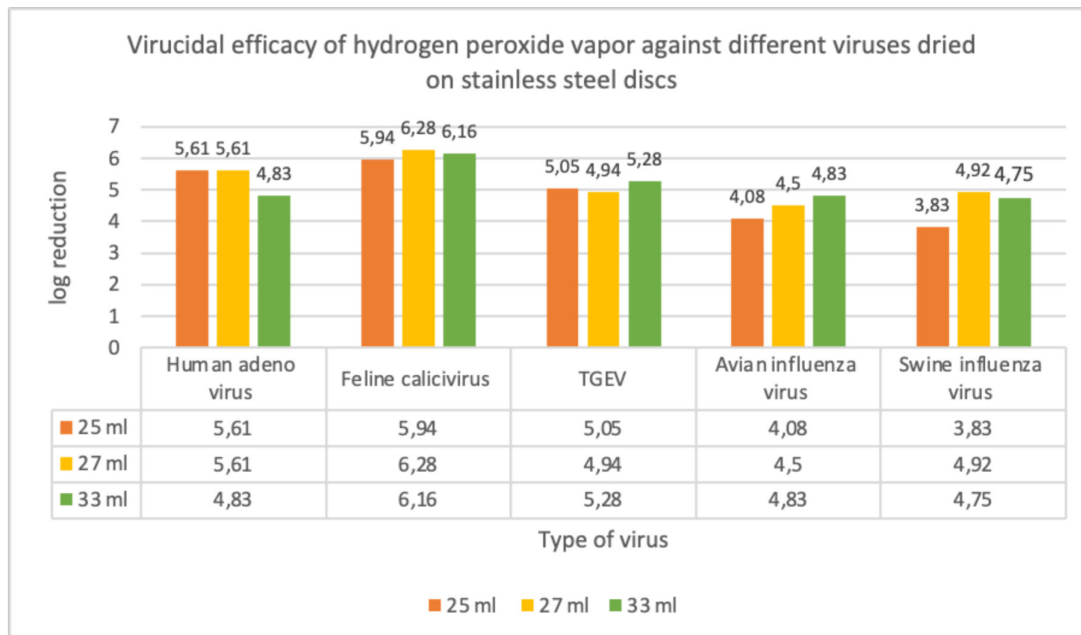


Figure 3. Virucidal efficacy of hydrogen peroxide against different viruses dried on the stainless steel surface

have been tested to ensure the effectiveness of disinfection. The effects of repeated VHP application on the permeability, morphological features, and fabric unity of the coveralls and N-95 masks were further evaluated. Their experimental studies revealed that in <10 min, one VHP cycle (7-8% H₂O₂) can effectively disinfect PPE and repeated treatment with VHP did not cause any morphological tear, malformation, or other visible alteration in N95 masks or coveralls. They believe that VHP treatment can also be successful against less tolerant groups of microorganisms, such as SARS-CoV-2 viruses. Therefore, approximately 2000 PPE bodysuits, which were used in COVID-19 hospital areas, have been successfully processed with a post-disinfection recovery rate of >80%^[59].

Furthermore, the use of H₂O₂ vapor can be an efficient way of decontaminating important surrounding areas, such as isolation systems, hospital rooms, technological devices, and pathogens-contaminated areas in general (Figure 4). Andersen et al.^[60] examined the effectiveness of H₂O₂ in the decontamination of rooms, ambulances, and medical devices in hospitals. According to the volume of the garages and rooms, they used an H₂O₂ dry gas device programmed at a pre-set concentration of 12-60 ppm per application cycle. For repeated tests (using *B. atrophaeus*), 1-3 cycles were used, accompanied by increased contact times of 30, 60, and 120 min, sequentially. Decontamination was successful using the three decontaminating cycles in 87% of 146 tests in special test rooms and 100% of 48 tests in the rooms of the surgical department.

Conclusion

In most hospitals, chloride disinfectants are commonly used, but thorough manual sanitation of surfaces may be insufficient to completely control the contaminants or virus transmission. Moreover, chloride gas can cause severe damage to humankind and the environment. Therefore, alternative methods with better performance and fewer side effects should be replaced. These alternative methods include UV radiation, H₂O₂, ozone, and CP. The potency of these substitute approaches against SARS-CoV-2 has been proven, and utilization of these techniques does not lead to acute problems, which are usually caused by chlorine-based disinfectants. Therefore, the application of these techniques is highly recommended for the disinfection of surfaces, air, and PPE to prevent the nosocomial transmission of SARS-CoV-2.

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Ethics

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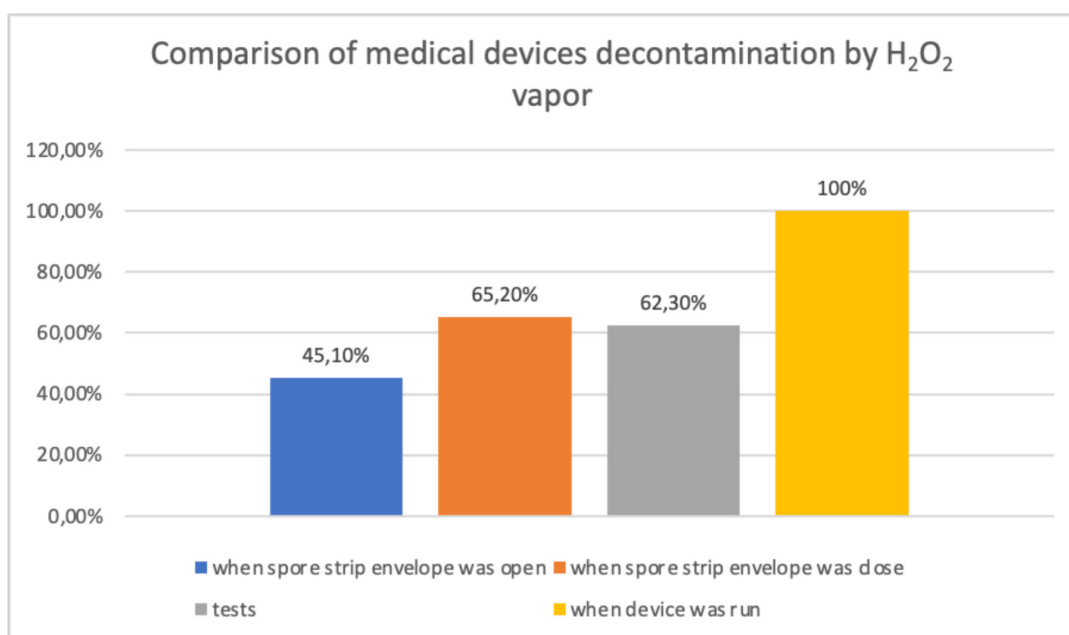


Figure 4. The comparison of medical devices decontamination by hydrogen peroxide vapor

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