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Sys Rev Pharm 2021;12(1):579-592
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The Role of Immune System and Sterilization on the Covid-19 Spread Control

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ABSTRACT

In the early first months of 2020. The WHO declared that the COVID-19 is a global pandemic. Which is spread rapidly across the majority of the continents all over the world. This dangerous virus infects the respiratory system. Leading to severe cases, to necrosis in the lung and difficulty in respiration pain and defect in kidney. Some cases recovered from this disease and other led to death. This review aims to clarify the role of the immune system in defending and confronting the disease, with pointing at the knowledge and the important aspect in sterilization disinfection to prevent and protect from exposure to infection.

Keywords: Immune system, sterilization, disinfectant, COVID-19

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INTRODUCTION

Viruses are intracellular parasites, which must get a preferred path to penetrate a susceptible host cell via the cell membrane and manipulate normal cellular processes such as sterilization and discovery of the correct action of nucleic acids to trigger a human body infection cycle[1,2]. At the end of 2019, a major global outbreak and public health problem was triggered by the emergence in China of the serious acute coronavirus 2 (SARS-CoV-2; previously referred to provisionally as the novel 2019 coronavirus or 2019-nCoV) disease (COVID-19)[3]. The data of the World Health Organization (MHO) as of 14th of June 2020 showed that in 215 countries / regions over 7,891,289 confirmed cases were reported, with over 432,746 death as listed also by Johns Hopkins University. The first case of novel coronavirus COVID-19 was reported in Wuhan, China, on 31st December and was declared on 30 January 2020 ton 6th international public health emergency by the WHO. SARS-CoV-2 has a close relation to the two acute coronaviruses bat-based, bat-SL-CoVZC45[4]. Coronaviruses are a group of non-segmented, single beached, positive RNA viruses. In addition to infecting a number of economically significant vertebrates (e.g., pigs and chickens), six coronaviruses infect and cause respiratory problems in human hosts. Severe ARTS (SARS-CoV) and Middle East Respiratory Syndrome (MERS-Cov) are zoonotic and extremely pathogenic, resulting in global and worldwide outbreaks of coronavirus., Coronaviruses have single-seam RNA virus genomes in the size range of 26 to 32 kilobases, the largest known RNA virus genome, which are nonsegmented and positive-sensitive. The virus has a core protein is involved in multiple viral replications. In particular, the carboxy terminal domain CTD is initially phosphorylated at multiple sites to facilitate viral RNA packaging into immature nucleocapsids (NCs) and the early stage of viral DNA synthesis[5]. The Virion contains the nuclear capsis of Genomic RNA and phosphorylated protein that is present in two separate spike proteins, the spike glycoprotein trimmer found in all CoVs virus; and hemagglutinin-esterase (HE) found in some CoVs [6]. The virion is present in two different types of spike proteins. Protein of membrane and of glycoprotein type III transmembrane[7]. After an incubation time of about 5.2 days, COVID-19 symptoms emerge[8] . The time from the onset of COVID-19 symptoms to death ranged from 6 to 41 days with a 14-day mean, which depends on the patient's age and immune system status of the patient. It is shorter among patients > 70 years of age compared to those less than 70 years of age[9].

The lungs are in contact with our environment on the largest surface within the human body. Such cells are passed through large quantities of air and aerosols each day, whereby the pulmonary tissue and other respiratory tract are likely to be nearly continuously exposed to inhaled air viruses and bacteria. An elaborate system, including mechanical obstacles such as a mucus layer, is therefore present in this large surface to protect this tissue against invading pathogens. Overactive immune responses, however, can cause immune conditions. Inhibiting viral replication and dissemination is important for the host system's response to viral infection by mediating inflammation and cellular antiviral activity. Excessive immune responses along with the virus lytic effects on host cells can, however, contribute to pathogenesis. Studies found that the common symptoms of disease onset were seriously affected by pneumonia, including fever including dry cough[10-13]. Some general COV virus description was reported by Rozhgar A. 2020 [14] that the length of the SARS-CoV genome is over 30 Kb, while just a few coding genes appear not to accord with the general properties for the viral genome and the minimum grouping of hereditary data. More on Coronavirus information was reported elsewhere [15,16]. Coronavirus particle are an enveloped, non-segmented, positive-sense single-stranded RNA virus genomes in the size ranging from 26 to 32 kilobases. The COVID-19 virus has a nucleocapsid composed of genomic RNA and phosphorylated nucleocapsid protein, which is buried inside phospholipid bilayers and covered by the spike

glycoprotein trimmer. The membrane protein (a type III transmembrane glycoprotein) and the envelope protein are located among the spike proteins in the virus envelope. This review article focused on the role of the immunological component against infection and its possible damaging effect on respiratory and other tissue injuries and Since CoV infections cannot be cured by any therapy or vaccine at least for the time of writing this report. The role of optimized antiseptic disinfectant is necessary, the efficiency of which is reviewed also.

I. Immune System

a. Defensive role of the immune system against infection

The immune system refers to a series of cells, chemical substances and medications that protect the skin, respiratory tracts, the digestive tract and other regions from external antigens such as bacteria, viruses, cancer cells, toxins and many others. Therefore, in a simple way, the immune system has two "protection lines, inborn immunity and adaptive immunity[17]. The structural and chemical barriers that defend as against infection. The first line of defense against an intruding pathogen is innate immunity. This is a non-specified antigen defense mechanism that the host uses immediately or within hours of an antigen. The innate immune reaction does not have an immune memory, which means that if it's actually exposed to it, you cannot remember or "memorize" the same pathogen. Anatine-dependent and antigen-specific adaptive immunity, meaning that there is a time delay between antigen exposure and a maximum response. The characteristic feature of adaptive immunity is the memory capability which allows the hosts to respond more quickly and efficiently to their antigen exposure. Innate and sufficient immunity is not shared[18-20]. The pulmonary epithelium is the largest surface area of the human body of contact. Massive quantities of air and aerosols pass these cells all time, which almost continuously exposes both the lung tissue and the rest of the breathing system to inhaled air viruses and bacteria. An elaborate system, with mechanical barriers such as a mucus membrane, is therefore present at this broad surface to protect this tissue against invading pathogens. This novel coronavirus causes severe acute respiratory syndrome similar to the SARS pathogenic coronaviruses. The virus ridded over the first line of protection in the tract is the innate immune system from the Nasopharynx to the alveolar membrane [21-23], the aberrant immune-inflammatory response and cytokine may play an important role in the disease progression.

b. Efficiency of the immune system and its components against Coronaviruses

The cells and functions of the innate immune system are confronted by micro-organisms or toxins that successfully penetrate an organism. The innate immune response is typically caused by the detection of microbes by pattern recognition receptors[24] that recognize components retained across large classes[25]. Innate immunology defenses are not specific, these mechanisms mean that the pathogen responds in a generic way to pathogens, or when injured or stressed cells send warning messages, many of them (but not all) are recognized by the same receptors as pathogens recognizes. The long-term immunity to a pathogen cannot be established by this system. The innate immune system in most species is the dominant host defense system[26]. Toll Like Receptor TLRs are a protein class that play a key role in the innate immune system. They are one-pass membrane receptors normally expressed on sentinel cells as macrophages and dendritic cells that recognize molecules derived from microbes that are structurally preserved. Once these microbes breach the physical barriers such as the mucosa in the skin and intestinal tract, TLRs that cause immune cell reactions are established. Toll-like receptors TLRs are regulated by one of two adapter proteins, (Myeloid differentiation primary responses 88) MyD88 or (Domain containing adaptor-inducing interferon β) or (Domain containing adaptor-inducing interferon β) TRIF[27], but are not included in, TLR1, TLLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8. TLR9, TLR10, TLR11, TLR12 and TLR13[28]. The TLR response activation results in a signaling cascade to kill and eliminate the invading pathogen[29] the ability of the immune system to recognize pathogens-share molectibes in part is due to the presence on the leukocyte membranes, including dendritic cells, macrophages, natural killer cells, adaptive immunity cells T cells and B Cells as well as non-immune cells (epithelial and endothel cells) of immune system receptors called toll-like receptors[30]. Dimerizing TLRs induces a cascade of TLR signals to trigger expression in various genes such as cytokines, chemokine's, mono-histocompatibility complex (MHCs) and co-stimulatory molecules that involve the Hosts immune function following the formation of TLR and (pathogen related molecular patterns) PAMP molecules complex[31] TLRs are connected to the ligand by their extra-cytoplasmic repeated motifs in the (Leucine-rich repeated) LRR domain. Different adapter molecules like RIF, (Toll interferon type1 receptor domain containing adaptor protein) TIRAP and/or TRAM, which can contribute to activation of (Intra-cellular signaling pathway), Nuclear Factor kapa B (NFμB) and Interferon regulated factors (IRF) signaling are recruited from its intra-cytoplasmic TIR domain. All of which signal via the type I cytokine receptors that are structurally divergent from other cytokine receptor types. By contrast, the critical pro-inflammatory chemokine, IL-8, signals via G protein-coupled receptors (GPCRs)[31,32]. Depending on the adapter molecule, MyD 88 and MyD88 independent / TRIF based pathways are recruited TLR in two separate pathways[33,34]. Cells have pattern recognition receptors in the innate immune system that detect infections or cytosol damage. A three primary classes namely Nucleotide-binding oligomerization domain-containing proteinNOD receptors, retinoside acid-inducible gene RIG receptors and cytosol DNA sensors are these cytosolic receptors[35]. Inflammatory substances are play a defenses role, these are metameric complexes formed by a number of physiological and pathogens. The activation of the inflammation is a critical component of the inborn immune response and is necessary for pathogens or damaged cells to be clear. However, open inflammatory activation is also a main driver of auto-immune and metabolic disorders, illustrating the importance in physiological and pathological contexts of understanding this mechanism[36]. Recent developments have been discussed in detail[37,38]. In our understanding of inflammation activation mechanisms, but to better understand its relation to disease, we offer a brief overview of the recent developments in inflammation activation mechanisms. Inflammation are multimeric protein complexes which are assembled after PAMPs or DAMPs are detected in the cytosol[39,40]. Although the immune system is important for wellbeing, the immune system may be activated unnecessarily and/or chronically, causing activation of the body's cell itself,

which can result in activation-related immune conditions[41,42]. The main molecules for this response are interferons (IFNs). There are three interferon families; Type 1 interferons have a broad antiviral activity *in vitro* and are currently evaluated in a clinical trial to treat MERS-CoV. There is a preliminary data concerning the potential activity of type 1 interferons on SARS-CoV-2, and the relevance of evaluating these molecules in clinical trials for the treatment of COVID-19.) [43,44]. There is a dual nature to these cytokines as has been demonstrated that both type I and type II IFNs have immunoregulatory functions during infection and type II immune responses. this response to minimize tissue damage[45]. Type III IFNs in several different cell types are considered the major antiviral innate actors, while Type II IFNs are expressed by more limited immune cells, which modulate adaptive immunity. type I (IFN-β) and type III (IFN-λ) are stimulated genes in patients with chronic rhinosinusitis with and without nasal polyps[46]. The Type I and III IFNs are Stimulated Genes triggered by which support anti-viral status in infected and surrounding cells, restrict viral replication, and lead apoptosis to protect the organization against virus propagation[47,48]. Type I and III IFNs are induced quickly to activate antiviral condition during viral infections. The IFN family type I comprises 13 subtypes of IFNα (in human beings). There is also one subtype of IFNβ and a few poorly studied subtypes[47,49]. IFNβ family is the same as IFNα subtypes (in humans). IFN-μ1, IFN-μ2, IFN-μ3 and IFN-μ4 are a newly discovered Type III IFN. In turn, both types are similar in the trigger for type I and III, IFN development and downstream signaling molecules[50,51]. IFNα therapy with steroids was related to improved levels of oxygen saturation and a quicker improvement of lung defects in patients that develop acute respiratory distress syndrome infected by human SARS-CoV[52]. Treatment with IFN~ in combination with ribavirin led to an increased survival rate of 14 days following diagnosis in patients with a MERS-CoV infection. This effect was no longer present after 28 days, in other studies have concluded that there is no beneficial impact as reported[53-57]. Innate immune cells must identify the virus invasion, mostly by pathogen-related molecular patterns (PAMPs), to mount an antiviral response. RNA viruses such as coronavirus are known to have either endosomal RNA receptors, TLR3 and TLR7 or cytosolic RNA sensor, RIG-I / MDA5. TLR3, which is specific for double-stranded RNA and normally recognizes virus-infected cells in the body in the form of viral genome RNAs or intermediates during viral replication, like dsRNA[58]. The recognition event causes the downstream signal cascade to be triggered, that is to say. Their nuclear translocation is followed by (nuclear factor) NF-Fraction and (inter-regulatory factors) IRF3. These transcription factors induce IFN and other pro inflammatory cytokines to be expressed in the nuclei and this initial response[59]. Type I and III IFNs are induced quickly to activate antiviral condition during viral infections. The big defenses of adaptive immunity, in the event of inborn immunity of removal the infectious agents are important to establish the adaptive immunity through the actions of the innate immune system. The key functions for adaptive immune response are recognize such "non-self" antigens, differentiate them from "self" antigens, establish pathogen-specific pathways of immunological effectors that eradicate pathogens or pathogen-infected cells and build an immunological memory which can quickly remove a particular pathogen. The foundation for specific effective vaccine against infectious diseases is adaptive immune responses[60-62]. Adaptive immunity has developed to give all self-antigens a more robust and finely tuned repository of knowledge. Adaptive immunity requires a closely mediated interplay between T and B lymphocytes and anti-antigens, which facilitates the production of pathogen-specific immune effector pathways, immune memory generation and host immune homeostasis. In a number of lymphoid organs forming the lymphoid system, lymphocytes grow and are activated. During the creation of gene segments, genes encoding different T and B antigen receptors are rearranged and assembled. The process for rearranging is enormous[63]. Adaptive immune response is essential to stop recurring infections caused by the same pathogen and preserve a memory. For the inhibition of viral infections. It takes several days to weeks to activate adaptive immune response to viral infections. This cycle includes certain antigenic cells Antigen presenting cells (APC) such as neutrophils (later differentiation into the macrophages of the muscles and dendritic cells that are the bridges between adaptive immunity) that control the co-stimulating molecules, such as CD80 and CD86, and pro-inflammatory cytokines, such as interferon (IFN), tumor necrosis factor (TNF), and interleukin (IL)[64-66]. Special forms of leukocytes, or lymphocytes, are the cells of the adaptive immune system. B cells and T cells are the major forms of lymphocytes originating from bone marrow hematopoietic stem cells. B cells engaged in a humoral immune reaction, while T cells engaged in cell-immune reaction[67]. There are two MHC defenses rout: Class I MHC antigens only are recognized by calls T-killer and Class II-MHC antigens are recognized only by T-cells and regulatory T-cells and important for the initiation of the antigen-specific immune response[68,69]. These two antigen presentation mechanisms illustrate the various functions of the two T-cell forms. The third a small, is a α-T-cell that is recognizing intact antigens as not bound to MHC receivers[70]. A large array of self-antigens in thymus in which joy is essential for thymic production and activity are exposed to double-positive T-cells[71]. In comparison, an antibody molecule on the cell surface of B is the antigen-specific receptor for B and detects whole pathogens without the need for antigen treatments. Lineage of B cell exhibits a specific antibody, so that all antibodies that the body can generate are expressed by a whole set of B cell antigen receptors[67].

II. Disinfection

a. The role of sterilization and disinfectant in virus infection

The viruses must be able to live in or on such vehicles as long as direct or indirect interaction with a susceptible host is possible before viral dissemination through infected environmental cars can take place. Hosts contaminated by body secretions and excretions release viruses into the world. The present organic matrices and cellular debris protect the viral agents from degradation outside the host and are directly proportional to the degree of viral survival. In preventing virus transmission by used disinfectants play a role whereby residual amounts of disinfectant chemicals are likely to be exposed to humans and animals. Some information about the latest coronavirus (COVID-19) causing disease is presented as the virus spreads mostly all over the world[72] by mechanism from person to person and contaminated surfaces. There are several ways this can happen such as droplets with the virus fly into the air and

aerosolized transmission. Research shows that the virus can live in the air for up to 3 hours.

1. Surface transmission

Another way to catch the new coronavirus is when you touch surfaces that someone who has the virus has coughed or sneezed on based on existing information about the new coronavirus and related coronaviruses that cause SARS and MERS, it is most common among near contacts (around 2 meters) that these viruses spread from one person to another. This transmission takes place via respiratory outlet. On the other hand, it has not been reported that new coronavirus is transmitted to people from virus-contaminated surfaces. Coronavirus transmission takes place much more frequently through respiratory gout than through fomites. Current evidence indicates that new coronaviruses can be maintained for hours. The structure of viruses is important and closely associated with intrinsic resistance to disinfectants and sterility[73-75].

A brief description of the key goal of infection prevention is to prevent transmission of pathogens or microorganisms[76]. Viruses are generally classified into two groups: enveloped viruses[77] (being sensitive to most disinfectants) and non-enveloped[78] viruses having a much higher level of resistance. It may persist on surfaces for several days or even months and can be transferred directly from contaminated surfaces to susceptible patients. The specific extent of resistance can vary depending on the virus strain as well as on the disinfectant[79]. Coronaviruses are enveloped viruses with a positive-sense single-stranded RNA genome that have several families such as SARA, MERS[80]. in which they are nucleocapsid of helical symmetry. The pathogenesis mechanism and diseases outcome of these virus are quite cleared to some degree, but less information available on the COVD-19[81]. The concentration of active antimicrobial chemicals present at use dilution influences the virucidifical properties of the disinfectors. The results that might be attributable to the design of the disinfectant dilution diluent, the quality and cleanliness of any porous applicators used and interactions between active chemical substances and the detergents or fillers used in the formulation are less evident.

2. Mode of action of disinfection

Disinfection is a way that can eliminates many or all pathogenic microorganisms or deactivates undesirable viruses on inanimate objects. Germs include living microorganisms, such as bacteria, fungi and viruses, which can cause infections or diseases mostly responding to disinfection. The disinfection process is depending on the amount achieved and type of germ destruction. The automated disinfection procedure is usually by dispersion of disinfectant on individuals by passing them through the disinfection chamber or tunnel. These chambers may activate by infra-red or any movement sensors. Several kinds of sprayers are used to disperse the disinfectant. The spraying process takes between 20 to 30 seconds for each round of disinfection. There was no retrievable scientific evidence on the effectiveness and safety of disinfection to reduce transmission of COVID-19. However, the disinfection is not that certain to replace existing strategies and control measures such as hand washing, social distancing, use personal protective equipment and high-level surface disinfectant to combat the spread of coronavirus[82]. Several disinfection modes and procedure are decried in the following subject.

b. Oxidation action

Such as halogen agents e. g. sodium hypochlorite in which can be used at ambient temperatures. Sodium hypochlorite is more stable in dilute solutions that contain solvated Na^+ and OCl^-, equation 1.

$$OCl^- + H_2O \rightleftharpoons HOCl + OH^- \qquad 1$$

Other example: Iodine and Hydrogen peroxide, Iodine (medical use) the antimicrobial action of iodine is quick and works at low concentrations, and thus it is used in operating theatres. Its specific mode of action is unknown. It penetrates into microorganisms and attacks particular amino acids (such as cysteine and methionine), nucleotides, and fatty acids, ultimately resulting in cell death. It also has an antiviral action, but nonlipid viruses and parvoviruses are less sensitive than lipid enveloped viruses. Iodine probably attacks surface proteins of enveloped viruses, and it may also destabilize membrane fatty acids by reacting with unsaturated carbon bonds[83]. Hydrogen peroxide is formed in humans and other animals as a short-lived product in biochemical processes and is toxic to cells. The toxicity is due to oxidation of proteins, membrane lipids and DNA by the peroxide ions. The class of biological enzymes called superoxide dismutase (SOD) is developed in nearly all living cells as an important antioxidant agent. They promote the disproportionation of superoxide into oxygen and hydrogen peroxide, which is then rapidly decomposed by the enzyme catalase to oxygen and water[84].

1. functions of oxidation agents on DNA and RNA controls

Hydroxyl radical and hydroxyl ion are formed when hydrogen peroxide takes one electron from ferrous ion[85], when iron in human body intervenes in a Fenton reaction that promotes this situation further[86], see the following equations.

$$\longrightarrow \quad H_2O_2 \quad OH^- + OH^\bullet \qquad 2$$

$$\longrightarrow \quad Fe^{2+} + H_2O_2 \quad Fe^{3+} + HO^\bullet + OH^- \qquad 3$$

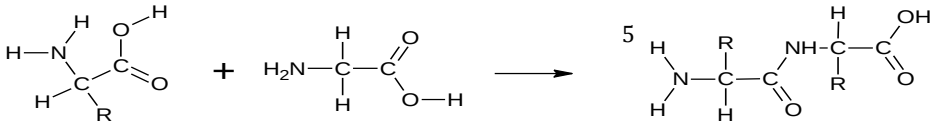
$$\longrightarrow \quad Fe^{3+} + H_2O_2 \quad Fe^{2+} + HOO^\bullet + H^+ \qquad 4$$

These radicals are damaging DNA and RNA strands, or attack purine or pyrimidine phosphate backbone and ribose or deoxyribose. For instance, when a hydroxyl radical attacks thymine, it becomes a thymine glycol. A broken thymine can be defined as the thymine glycol. The damaged thymine is not able to carry out its tasks as a nucleic acid, such as replication, transcription and translation. It attacks the sugar (deoxyribose) of DNA, forming and breaking the foundation of deoxyribonolactone[87]. A low concentrations of hydrogen peroxide, such as 6%, are widely available and legal to buy for medical use. Higher concentration is an aggressive oxidizer and will corrode many materials, including human skin. In the presence of a reducing agent, high concentrations of H_2O_2 will react violently so high-concentration hydrogen peroxide streams, typically above 40%, should be considered hazardous[88]. An experimental study using 5%, 10% and 35% was conducted. Thirty-five percent hydrogen peroxide showed greater efficacy and speed to achieve full kill over a period of 60 min while 5% can perform after more than 3h[89].

2. Effect oxidation disinfection agent on proteins or amino acids

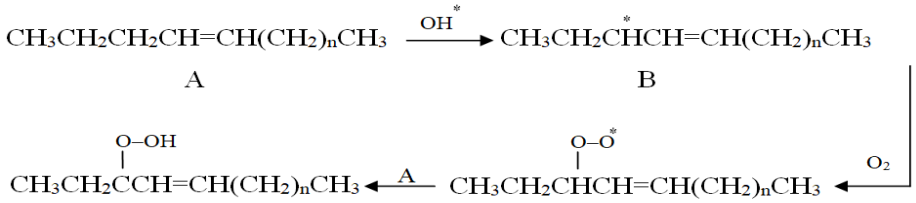
The bond splits when the oxidizing agents take an electron and act on a peptide bond. The structure is thus

deformed and therefore cannot normally operate. This is especially fatal if an enzyme is impaired. Therefore, in living organisms, the process is normally catalyzed by enzymes known as peptidases or proteases and due to peptide bond hydrolysis caused by conformational strain as the peptide/protein folds into the native structure. Amino acids or proteins have also been damaged. This non-enzymatic process is thus not accelerated by transition state stabilization, but rather by ground state destabilization. Due to this reaction produces a molecule of water and two amino acids joined by a peptide bond (-CO-NH-). The two joined amino acids are called a dipeptide hence the process is a dehydration synthesis reaction[90], equation 5.



3. Effect on lipids content

Lipid peroxidation is the oxidative degradation of lipids or lipid oxidation products (LOPs). It is the process in which free radicals "steal" electrons from the lipids in cell membranes, resulting in cell damage. They strike double bonds if more electrons extracted[91]. Oxidants break lipids down into smaller fastidious acids, preferring the unsaturated fatty acids. This kills the cells and produces more radicals, which aggravates unsuitable condition. By lipid peroxidation, the cell then collapses, and the contents break down. The cell wall and membrane flexibility are lost. Since the lipids contain multiple double bonds in between which lie methylene bridges (-CH_2-) that possess especially reactive hydrogen atoms and become subject to saturation or hydrogen substitution[92]. As with any radical reaction (scheme1), the reaction consists of three major steps: initiation, propagation, and termination. In particular, a high hazard manifested if the oxidation process is not terminated fast enough, which consists mainly of lipids[93]. In recent years, development of immunochemical detection of HNE-histidine adducts opened more advanced methodological possibilities for qualitative and quantitative detection of lipid peroxidation in various human and animal tissues as well as in body fluids, including human serum and plasma samples[94].



Scheme 1

c. Non-oxidants action

The nonoxidant agent such as alcohol, biguanides (chlorhexidine), quaternary ammonium compounds, phenol, aldehyde (glutaraldehyde), and ethylene oxide are under category no oxidation disinfections. The action mechanism of these compound is all linked to coagulating ingredients[95].

1. **DNA and RNA controls by alkylating agent**

The process of adding an alkyl group to the guanine base of the DNA molecule called alkylating agents. These compounds are working by preventing the DNA and RNA strands of the double helix. The alkylating agents work on the molecules of DNA or RNA by cross-linking nucleotides or introducing single strand by breaks DNA double-helix strands via attacking DNA directly. This makes the strands unable to uncoil and separate. In addition, these agents interconnect structures to neighboring nucleotide bases and induce disorder. There is also no proper separation of DNA strands, which is the first step in DNA reproduction and eventually blocks on proteins or amino acids[96].

2. **Action on amino acids or proteins**

When a cell surface expose to aldehyde a cross-linked cab be formed. Amino acid functional group (-NH_2) particularly of lysine, asparagine, glutamine, and arginine are more preferable for such cross-linkage. This triggers a degradation of the protein structure when nucleic acids and lipid structures are balanced[97].

d. Oxidation agent for disinfection

1. Chlorine Compounds

Chlorine is the most widely used halogen as a disinfectant, since it is highly resistant, fairly residual toxic to most vegetative bacteria. It can be manufactured in large quantities in a very low cost. In terms of termination treatment of drinking water and as sanitizers for commercial, institutional or home applications, chlorine compounds (particularly hypochlorite) are widely used in the food-and dairy industries. Both the hypochlorite acid and the hypochlorite ions are formed by aqueous chlorine solutions. Though chlorine's exact mechanism of action is not well known, chlorine's lethal effect on micro-is commonly seen as a consequence to the formation hypochlorous acid. It has not been elucidated the exact mechanism by which free chlorine kills microorganisms. But the negative charge of cell walls around bacteria play the role by repelling other negatively charged particles in the water. The hypochlorous acid is neither positively nor negatively charged so it can make contact with and rupture bacterial cell walls. Chlorine inactivation can be the result of a number of factors: Sulphur enzyme oxidations and amino

acids; amino acid ring chlorination; intracellular intake losses; nutrient uptake decreases; protein synthesis inhibitions; lower oxygen uptake; respiratory oxidation part oxidation; lower adenosine triphosphate manufacture; DNA breaks; and depressed DNA synthesis. The action of organochlorine mechanism is by their aqueous solution for releasing hypo-chlorinated acid; there was also a suggestion for an alternative scheme for the direct transfer of chlorine. The active species is neutralized, and the equilibrium re-established, thereby raising the amount of hypochlorinated acid is freed up. mono-and dichloramine and halazone, are mainly used in the food and dairy industry as sanitizers. For household and commercial bleach and cleaner, the chlorinated isocyanurates are especially used in disinfecting swim[98]. Organochlorines containing =N-C1 group, such as mono- and dichloramines, halazone and chloroisocyanurates, are also used as disinfectants. There was also a suggestion for an alternative scheme for the direct transfer of chlorine. The active species is neutralized, and the equilibrium re-established, thereby raising the amount of hypochlorinated acid is freed up. For household and commercial bleach and cleaner, the chlorinated isocyanurates are sanitizing ingredient especially used in disinfecting swim pools, spas and automatic dishwasher detergents and many other cleaning products[99]. Many experiments have been carried out on chlorine disinfectant of viruses. As chlorine is used for terminal treatment in drinking water, a certain degree of detail has been studied for the disinfection of enteric viruses which are usually present in the water from the sewage contamination source. These enteric viruses are amongst the most stable and respond to chlorine problems, even if prepared in similar conditions.

The hypochlorite-based disinfectant is able to inactivate viruses. These are sodium hypochlorite, glutaraldehyde, or hydrogen peroxide/peroxyacetic acid as were investigated[100] on viruses below the assay detection limit. In fact, sodium hypochlorite is not spore-killing at daily levels, but sporicidal at or above 5,000 ppm. The concentration is 50,000 ppm for 5% sodium hypochlorite products. 5,000/50 thousand= 1/10 to reach 5,000 ppm. Thus, if 1 mL sodium hypochlorite is mixed with 10 mL water, it is possible to obtain 5,000 ppm. Because one cup is 10 ml in size, the liquid crude sodium chlorite is poured into the container, which then has been added to 1 liter of water. The comparison point is to sterilize fruits and vegetables at 100 ppm for 5 minutes, sterilize tableware at 200 ppm, and sterilize the cleaning of the floors in general at 400 ppm.[101]

2. Iodine compound

The study of iodine activity in an aqueous or alcoholic solution is important to understand the effects of iodine-containing disinfectants. The goods that contain iodine are primarily used for intact or damaged skin antiseptic. Recently, iodine monochloride was introduced as an inert surface disinfectant. Iodophors (complexes associated with iodine with a solubilizing agent or carriers, iodophors (5% and 10%,)[102] are also identified as products with iodine. They are good disinfectants on broad spectrum of antimicrobial, but they are less effective against sporogenous bacteria and viruses. The galenics type formulation dictates the bactericidal function of these materials. Iodine functions by reducing aerobic microorganism's oxygen needs. Iodine interferes at the microorganism's respiratory chains level by blocking electron transport with the enzymes of the respiratory chain by electrophilic reactions. Iodine also interacts ideally in form of a positive (H_2O^{+1}) or neutral (I_2 or HOI) charge with cytoplasm membranes proteins[103]

3. Hydrogen peroxide

Peroxides are an essential part of bacterial cell degradation. Bacteria such as *E Coli* are active in the presence of oxidants such as peroxides. Hydrogen peroxide (H_2O_2) does not effectively destroy low-level (< 2 percent) spores but behaves like a high-level disinfectant or chemical disinfectant where time at high concentrations is required (7.5-30 percent) protect itself by developing enzymes that either kill the oxidization agent before bacterial degradation occurs or aid the mechanisms of restoration. Oxidized molecules are more susceptible to proteolysis than others, and a 'cell-sanitisation system' has been proposed for the use of an oxidizing agent such as H_2O_2[104].

d. Non-oxidant compound on disinfection agent

Alcohols

Alcohols operate by cellular membrane disruption, lipid solubilization, and protein denaturation by working in the S-H functional groups directly. The two most widely used alcohols for their biocidal function are ethyl and isopropyl alcohol. These alcohols are useful in general, but not useful against spore-forming bacteria, in combating lipid viruses and a large array of bacterial organisms. They evaporate quickly and it is difficult to achieve extended contact times without immersing the objects.

1. **Methyl alcohol (methanol)** has the weakest bactericidal action of the alcohols and thus seldom is used in healthcare.

2. **Ethyl alcohol (ethanol**)

It is an effective antiseptic and can be used for a number of purposes in different concentrations. It can be used as antiseptic, preservative, mild counter-irritant solvent. It is widely used in hand rubs, gels, and foams for hand hygiene in healthcare settings. Ethanol at 80% (v/v) has even listed as an essential medicine in the category for hand rub as recommended by The World Health Organization. In certain circumstances with a high incidence of infectious disease and during infectious outbreaks virus, activity of the hand rubble is of significance denaturation and coagulation of proteins is the underlying process of ethanol. Ethanol has been shown to be effective against various enveloped viruses. Starting with concentration of 42.6% (w/w) shows its effectiveness within 30sec against SARS coronavirus, MERS coronavirus, ebolavirus, influenza A virus including the human type H3N2, the avian type H3N8 and human type H1N1, influenza B virus, HIV, HBV, vaccinia virus, duck hepatitis B virus, togavirus, pseudorabies virus, Newcastle disease virus, bovine viral diarrhea virus, zika virus, herpes simplex viruses type 1 and 2 and RSV [5,14e35]. Ethanol is effective at 73.6% (w/w) against HCV in 15 s and 30sec but not at 40%[105]. The basic structure of alcohols is a hydroxyl group (-OH), binds to a hydrogen protein bond and compromises the structure and function of proteins resulting in the inhibition and deposition of proteins. It's not sporicidal, it is involved in sports., at concentrations of 60%–80%, is a potent virucidal agent inactivating all of the lipophilic viruses (e.g., herpes, vaccinia, and influenza virus) and many hydrophilic viruses (e.g., adenovirus, enterovirus, rhinovirus, and rotaviruses but not hepatitis A virus (HAV) or poliovirus). The only alcohol that has been

tested to inactivate all of the viruses has been found to be ethanol at the minimum level of 70%[106].

3. Chlorhexidine

also known as chlorhexidine gluconate (CHG), is a disinfectant and antiseptic that is used for skin disinfection before surgery and to sterilize surgical instruments. It may be used both to disinfect the skin of the patient and the hands of the healthcare providers. It is also used for cleaning wounds, preventing dental plaque, treating yeast infections of the mouth, and to keep urinary catheters from blocking. It is used as a liquid or powder[107]. A formulation of 2% (w/v) chlorhexidine gluconate (CHG) in 70% (v/v) isopropyl alcohol (IPA) (ChloraPrep), was tested against Staphylococcus epidermidis RP62A in the presence or absence of protein, utilizing quantitative time-kill suspension and carrier tests was demonstrated to reduced bactericidal activity. These results suggest that enhanced skin antisepsis may be achieved with 2% (w/v) CHG in 70% (v/v) as presented by[108].

4. Quaternary ammonium compound (QAC)

Quaternary ammonium compounds are a large group of chlorinated compounds. Some concentrated formulations have been shown to be effective in low-level disinfectants. Typically, QUATs do not exhibit efficacy against difficult-to-kill nonenveloped viruses such as norovirus, rotavirus, or poliovirus. Newer formulation of low-alcohol content is highly effective for broad-spectrum disinfectants with quick contact times (3–5 min) against bacteria, enveloped viruses, pathogenic fungi, and myco-bacteria[109]. The action mechanism of Quaternary ammonium compounds (QACs) is to bind irreversibly to phospholipids and membrane proteins, thus impairing the permeability of the membrane, (e. g. preoperative skin disinfection, mucous membranes application and noncritical surface disinfection). QACs are also good for rough surface cleaning and deodorization, as well as antimicrobial properties. The QACs affect lipids, which are enveloped and not non-entangled (including human immunodeficiency infection and HBV). A broad number of associated compounds are QCB-based products that induce disintegration and morphological changes of human HBV that cause infection loss. A few condensed formulations have shown that they are effective disinfectants at low levels. Quaternary ammonia, plus alcohol, with 200 ppm or more, has an impact against hard-to-kill viruses such as norovirus, rotavirus or polio. Current synergistic formulations of low alcohol are highly effective broad-spectrum disinfectants which are rapid (3-5 minutes) in contact with bacteria, enveloped viruses and pathogenic fungi, and mycobacteria[110]**.** The bacterial cells have two regions in their molecular structures, one hydrocarbon, water-repellent (hydrophobic) groups and the other water (Hydrophilic). The bacterial cell's ability to absorb these molecules determines the disinfection capability. These antiseptic surfactants are categorized as cationic, anionic, nonionic, and amphoteric compounds depending on the charge or absence of ionization of the hydrophilic community. The most effective antiseptics and disinfectants are the cationic agents, e. g. quaternary ammonium compounds (QACs). Often, they are called cationic detergents. A variety of disinfectant on chlorinated base aromatic such as Benzalkonium chloride, benzethonium chloride, alkyl dimethyl benzyl ammonium chlorides (C12-16), alkyl dimethyl benzyl ammonium chloride (C14 60%, C16 30%, C12 5%, C18 5%), Alkyl dimethyl ethylbenzyl ammonium chloride (C12-14), Alkyl dimethyl ethylbenzyl ammonium chlorides (C12-18) and no aromatic such as didecyldimethylammonium chloride, dioctyldimethylammonium chloride.

5. Glutaraldehyde and ortho-phthalaldehyde (OPA)

OPA is widely used for the disinfecting of medical equipment as safer alternatives to formaldehyde. Significant amounts or concentrations of these materials may cause adverse effects, including impact on the process of biological sewage treatment, potential risks to sewer health, solutions which contain the OPA can be neutralized with the use of glycine powder or an approved neutralizing agent. Active OPA must not be over 200 mg / L in the final concentration of the manufactured solutions. glutaraldehyde's biocidal activity results from its microorganisms, which change the RNA, DNA and protein synthesis, in sulfhydrate, hydroxide, carboxyl and amino groups. The glutaraldehyde mechanism is thoroughly investigated elsewhere[111].

Glutaraldehyde is used for heat-sensitive devices such as endoscopes and endocavity ultrasound transducers [112]. Glutaraldehyde is a dialdehyde that reacts readily under suitable conditions, especially protein, by both groups of free aldehydes. This is relatively stable in acidic aqueous solution, but much less active than at alkaline pH where biocidal activity rapidly loses. This possibly stems from irreversible polymerization. Glutaraldehyde is formed by the bond of glutaric acid with the two aldehydes. Aquatic glutaraldehyde solutions are acidic and are not usually sporicidal in this environment. Even with the use of alkaline agents at pH 7.5–8.5 will the solution become sporcic. The solution is "activated" (made alkaline). If triggered, the glutaraldehyde molecules polymerized at alkaline pH levels have a shelf life of 14 days. This polymerization blocks the active sites of GLMs responsible for their biocidal activities, encourages glutaraldehyde action by alkaline pH (7.5- 8.5) for sporicidal solution[113], but in such a situation the solution is less stable, polymerizes the molecule, and decreases the disinfectant function. Combined with the effect of alkaline pH, the addition of inorganic cations has been suggested to improve the efficacy of bactericides. To order to ensure a safe working environment, Glutaraldehyde exposure should be controlled[114]**.**

6. Glutaraldehyde and Formaldehyde

The extremely large operation of formaldehydes and glutaraldehyde are also known as chemical sterilant. Glutaraldehyde is used as a disinfectant and drug. Usually applied as a solution, it is used to sterilize surgical instruments and other areas[115]. According to several proposed mechanisms, glutaraldehyde biocidal properties have been clarified. It is interacting with amines and thiol groups like other aldehydes which are common protein functional groups. It is also possible linker as a bi-function[116]. Formaldehyde an organic compound with the formula CH_2O (H−CHO) is the (systematic name methanal), it is the simplest (R−CHO) aldehyde. This material is generally named by its resemblance and its interaction with formic acid. Formaldehyde was especially commonly used to produce inactivated viral vaccines in this regard. Some authors were pointed out that all of the viruses tested were susceptible to formaldehyde inactivation, although sometimes the reaction was stated to be fairly slow. Formaldehyde is a major precursor for many other chemical materials. Table 1 shows the best comparison of

glutaraldehyde and formaldehyde as best used as sterilizers[117].

Table 1. The comparison between glutaraldehyde and formaldehyde as it is best used as sterilizers.

	Formaldehyde	Glutaraldehyde
	Slow reaction	Rapid
	Reversible (in first 24hr with excess of water)	Irreversible
	Not good morphological picture	Good morphological picture
	Less effective at cross linking	More effective at cross linking
	Loss of enzyme activity is less	Loss of enzyme activity is more

III. Sterilization

The full elimination or degradation process of all types of microbial life means sterilization. Incineration is the clearest method of sterilization. Incineration is therefore not realistic, since a variety of instruments have to be recycled in the medical sector. The second-best way to avoid disease transmission related to the use is, therefore, to use the autoclave sterilization, which kills all microorganisms on the surface of a product or in a fluid. Although the use of critical elements inadequately sterilized presents a high risk of pathogens transmission, a reported pathogen transfer from an insufficiently sterilized critical component is fairly rare[118].

a. Mechanism of sterilization

The autoclave which operates under the same principle as a pressure cooker is a representative method for sterilization. The plasma or flame, which can work in ultra-high temperature settings, vapor and hydrogen peroxide[119].

b. Physical Sterilization

1. Autoclave

Autoclave is one of the most convenient and reliable means of sterilization possible at a temperature of 121°C (250 GF) and 15 to 20 psi. The time is estimated at 121°C (250°F) upon the sterilization material temperature. In order to ensure even heat distribution, care must be taken to ensure that steam can flow around objects. In liquid media, the effectiveness of the sterilization depends heavily on time dependent, with large quantities taking long time to reach the effective temperature inside the material. There should also be no gap places in the load to prevent the flow of heat from being insulated against steam. Moist heat kills microorganisms mainly proteins by denaturation of macromolecules. This method is quicker than sterilization by dry heat[120]. The heat is inactivating viruses through denaturation of secondary protein structures and alteration of the viral glycoprotein involved in the attachment of the virus to the host cells. In the examine the ability of heat to inactivate CCoV. It has been reported that CCoV is stable at 56°C for up to 30 min but tended to decrease rapidly at 75°C as has been reported[121].

2. Dry heat

Dry heat is the first sterilization method and is a longer than moist thermal sterilization cycle. Microorganisms are slowly killed by the use of dry heat. The number of killed microorganisms increases with prolonged exposure to lethal temperatures. Forced ventilation by hot air may be used to increase the heat transfer rate and lower the temperature and time necessary for sterilization. At levels above, cells will be killed in shorter exposure periods. This may damage to food products caused by heat[122]. It helps to turn air into the sterilized product rapidly. Surface properties like topography surface and energy of unalloyed Titanium implants can vary as a result of dry heat exposure. These changes in the characteristics of the implant surface can dramatically affect biological reactions. The primary lethal process during dry-heat sterilization is known to be oxidation of the cellular components, Bacterial endotoxin destruction is also stated to be a major lethal factor[123].

3. Flaming

Flaming fire is made in microbiology laboratories for streaking by inoculation loops and straight wires. Leaving a contagious agent in the flame of a brunette or an alcohol burner until it glows in blood. This is also used for small items in metal or glass, but not for large objects. During initial heating, however, infected material may be sprayed from the wire surface and contaminated with surfaces and objects nearby until they are destroyed. Special heaters that surround the inoculative circuit with a heated cage have also been designed to ensure that such sprayed content will not contaminate the region further.

Heating is a trustworthy way to extract objects from all the communications agent, but if heat sensitive material like biological materials, fiber optics, electronics and other plastics is harmed, it is not always suitable. For these circumstances, chemical products may be used as sterilant in either a gaseous or liquid form. In order to avoid the heat damage issue, the use of gas and fluid chemical sterilant must be ensured that the substance being sterilized is chemically compatible with the sterilizer used. Furthermore, the use of chemical sterilant poses new obstacles to occupational health, because chemical efficacy properties usually affect people.

c. Chemical Sterilization

1. Ethylene oxide

Gas treatment with ethylene oxide (EO, EtO) is one of the popular methods of sterilization, pasteurization or disinfection due to its broad range of compatibilities. This is often used for processing products that are sensitively treated using other methods like gamma, electron beam, electromagnetic radiation, heat, or other chemical substances (moist or dry). Ethylene oxide therapy is the most commonly used form of chemical sterilization for around 70% of overall sterilizations and for over 50% of all disposable medicines.(Kanemitsu et al., 2005) Ethylene oxide enters the cell, hits the DNA of the microorganism and destroys it by Alkylation, because of its function as a gas. It should be handled carefully because it can burst quickly, and typically frozen. Ethylene oxide is destroyed by the body and will require ample time for the body to work (6–12 hours) as a result of its drawbacks. It's also an environmental pollutant[124-127].

2. Nitrogen dioxide

Nitrogen dioxide is a sterilizing gas which is used when medical instruments are terminally sterilized. For the terminal sterilization of medical devices, traditional chamber sterilization systems have been validated with

the NO_2 sterilization cycle. Unique advantages are not available with other sterilant gases rather the NO_2 process. The advantages include room temperature operations, relatively low levels of sterilant, strong microbicidal activity and minimal residual sterilant on processed products. Such benefits allow the NO_2 method to be used in resource-efficient environments. Nitrogen dioxide is an ambient gas rather than a vapor that enables easy penetration. The cooking point of NO_2 is 21°C at sea, resulting in a saturated vapor pressure at room temperature that is fairly high (101,325 Pa). The NO_2 process also involves an environmental pressure gas concentration of about 1 percent, which is comparatively small in comparison with other gas sterilant. As a consequence, the amount of NO_2 in the sterilization process is well below the point of dwelling of NO_2 and there is no condensation of the sterilant. In addition, this gaseous form of NO_2 under environmental conditions ensures effective load aeration and safe handling of refined goods[128].

d. Radiation sterilization

Electromagnetic or specific radiation may be energetic enough to radiate or decrease energy (non-ionizing radiation) atoms or molecules, as well as electron beams, X-rays, gamma rays or irradiation by subatomic particles, It is usually High Energy Electron beam (beta-radiation), High Energy X radiation (brake-radiation), Gamma-radiation (Co^{60}) or Cs^{137}. Comprehensive protocols for confirmation, dose collection, and routine control for sterilization of tissue allografts by radiation are provided by the International Atomic Energy Agency (Vienna) [129].

1. Non-ionizing radiation sterilization

Irradiation of surfaces and certain transparent objects (UV, from a germicidal lamp) is beneficial for sterilization. Many transparent objects absorb ultraviolet light. Routine UV irradiation is used in biological protection cabinets to sterile the interior between uses, but it is ineffectual in shaded areas, including dirty areas (which may polymerise after long irradiation to make it hard to remove). Non-ionizing UV irradiation can be sterilized by this process, products of unstable composition. UV radiation is absorbed by nucleic acids in the bacteria. This results in cyclobutane dimers formed between thymine DNA residue and similar dimers between cytosines and thymine cytosine residue. Such stable dimers, irreversibly bound, inhibit replication and transcription, resulting in death[130].

2. Ionizing radiation sterilization

Gamma radiation is high and widely used as a sterilization of instruments like syringes, needles, cannulas and sets of IV and food. The use of gamma radiation is extremely high. The exterior walls are made of dense, reinforced concrete, for radiation protection, including roof. It is released by radioisotopes of up to 1,3 and 0,66 MeV of photonic energy, typically cobalt-60 and cesium–137. The Gamma irradiates essential cellular elements (notably nucleic acids), leading to microbial deaths[131]. In general, the process of gamma-inactivation of the virus falls into two categories: direct and indirect. Gamma irradiation leads to a direct inactivation of microbes primarily due to radiolytic slippage or genetic material cross-linking[132,133].

Indirect gamma irradiation effects are mainly associated with radicals such as· OH, which are caused by the radiological cleavage of water and ozone, which is formed by the radiolytic cleavage of O_2 to O and the reaction to it with another O_2 molecule. The molecules can react with both viral and protein nucleic acids. The destruction by direct and indirect mechanisms of replication of competent nuclear acids is assumed to be the key mechanism of inactivation of the virus by gamma irradiation, Scavengers, hydroxyl-radical and ozone reacting molecules and thereby blocking their ability to operate on viral nucleic acids or proteins, dampen the indirect effects of gamma-irradiation[134].

CONCLUSION

In order to prevent microbial infection, the immune system uses several approaches. Such mechanisms cooperate and the fully integrated immune response incorporates elements from several effector systems to adapt a response to the particular pathogen intrusion. Sterilizers and disinfectants are important and necessary in the prevention and avoidance of disease, but it is rewarded to develop these substances as a way to reduce and prevent infection with these causes, because these are always evolving from environmental impact and genetic mutations. Cleaning and disinfection must be fully effective, restricting contamination to an acceptable minimum level which is compatible with further manufacture.

ACKNOWLEDGEMENT

The authors thank University of Basrah, University of Al-Ameed for the support.

Author contributions

All authors contributed to writing of the manuscript. All of the authors approved the final version for publication and are sure of the aspects reported in this work.

COMPETING OF INTEREST

The authors declare no competing interests.

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