Review paper
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STRUCTURE AND PHYSICOCHEMICAL PROPERTIES OF ANTISEPTICS AND DISINFECTANTS IN RELATION TO THEIR ACTIVITY

Biljana Gorgeska[1*], Andonela Janeva[1], Ivana Iceva[1], Dino Karpicarov[1], Antonela Velkova[1], Viktorija Krzovska[1], Ana Dimitrova[1], Natali Delipetrova[2]

[1]Department of pharmacy, Faculty of Medical Sciences, Goce Delcev University,
Krste Misirkov bb, 2000, Stip, Macedonia
[2]Department of general medicine, Faculty of Medical Sciences, Goce Delcev University,
Krste Misirkov bb, 2000, Stip, Macedonia

[*]e-mail: biljana.gorgeska@ugd.edu.mk

Abstract

Antiseptics and disinfectants represent a large group of compounds that have different effects depending on the used concentration. They are substances that remove bacteria from the skin or materials and are part of the practices for infection control in hospitals.

The action of antiseptics and disinfectants is due to mutual reaction with the cell surface of the microorganisms, followed by their penetration into the cells and the influence on a certain target area. Intrahospital (inpatient, nosocomial) infections are localized or generalized infections caused by microorganisms acquired during hospitalization. Intrahospital infections also include recurrent infections acquired during other hospitalizations and other manifest infections in patients that move from one hospital to another. In fact, these infections can result from inappropriate use of antiseptics and disinfectants. The purpose of this study is to establish a correlation between the mechanism of action of antiseptics and disinfectants and their chemical structure.

This correlation may be the basis for creating an approach that will be used as prevention from the occurrence of intrahospital or nosocomial infections. The establishment of such an approach is crucial because it is necessary to know which antiseptic or disinfectant has the greatest activity against the microorganism which is the cause of the intrahospital (nosocomial) infection.

Key words*: Antiseptic, Disinfectant, Prevention, Microorganism, Intrahospital infection.*

1. Introduction

Antiseptics and disinfectants represent a large group of compounds: alcohols, aldehydes, anilides, biguanides, diamines, halogen release agents, silver compounds, peroxides, phenols, bis-phenols, halophenols, quaternary ammonium compounds, volatile compounds for sterilization. Antiseptics and disinfectants are labeled as biocides.

Biocide is a general term describing a chemical agent, usually a broad spectrum that inactivates microorganisms. Because biocides range in antimicrobial activity, other terms may be more specific, including "-static", referring to agents that inhibit growth (e.g.: bacteriostatic, fungistatic and sporiostatic) and "-cidal", referring to agents that kill the target organism (e.g.: sporicidal, virucidal and bactericidal) [1].

The main difference between antiseptics and disinfectants is the place of application. Namely, antiseptics are biocides that have the ability to destroy microorganisms or prevent their growth, development and reproduction when applied to living tissues, and disinfectants are biocides that have the ability to destroy microorganisms or prevent their growth, development and reproduction when applied to a variety of objects and equipment, or to remove pathogens from the immediate environment. If we take into account that antiseptics and disinfectants possess a different chemical structure, it is freely to conclude that sometimes that chemical structure is decisive for their effect. Therefore, it is necessary to establish a correlation between the chemical structure and the activity of antiseptics and disinfectants.

Antiseptics and disinfectants can be used as a suitable way for the prevention of intrahospital (nosocomial) infections, which can cause serious problems in modern medicine. Irregular and irrational use of antiseptics and disinfectants may result in the appearance of this type of infection.

A nosocomial infection is one for which there is no evidence that the infection was present or incubating at the time of hospital admission. To be classified as an infection, the condition must be manifested as a clinical disease and not a colonization, which means that microorganisms are present but have no adverse effect on the host. However, an asymptomatic patient may be considered infected if pathogenic microorganisms are found in a body fluid or at a body site that is normally sterile, such as the cerebrospinal fluid or blood [2].

Disinfection removes microorganisms without complete sterilization to prevent transmission of organisms between patients. Disinfections procedures must [3, 4, and 5]:

- Meet criteria for killing of organisms.
- Have a effect similar like surfactants.
- Act independently of the number of bacteria present, the degree of hardness of the water, or the presence of soap and proteins (that inhibit some disinfectants).

To be acceptable in the hospital environment, they must also be:

- Easy to use.
- Non-volatile.
- Not harmful to equipment, staff or patients.
- Free from unpleasant smells.
- Effective within a relatively short time.

Antiseptics and disinfectants are integral part of the hospitals because they are widely used in the hospital departments. It is very important to use the right antiseptics for the treatment of certain infections and the right disinfectants for removal the microorganisms from the medical equipment used in diagnostics and surgery. As a result of that, the occurrence of intrahospital infections will be minimized.

2. Structure and physicochemical properties of selected antiseptics and disinfectants in relation to their activity

The following is a review of the literature on a topic which has been continuously evolving. The most commonly used antiseptics and disinfectants in the researched hospitals are: ethanol (alcohols), pividone iodine (halogen release agents), formaldehyde (aldehydes) and hydrogen peroxide (peroxides).

2.1 Ethanol solution

The ethanol solution used as antiseptic and disinfectant contains ethanol in water in different concentrations. The ethanol is clear, colorless liquid that has bactericidal activity and is used often as a topical disinfectant. It is widely used as a solvent and preservative in pharmaceutical preparations.

Ethanol structure is presented in Figure 1.

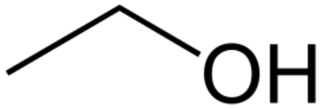

Figure 1. Chemical structure of ethanol

The molecular formula of this chemical compound is CH_3CH_2OH or C_2H_6O. When it comes to the physicochemical properties, the ethanol is colorless, clear volatile, flammable liquid, which is also hygroscopic. It is miscible with water and with methylene chloride and also, it burns with blue, smokeless flame. The boiling point of ethanol is about 78 ^{0}C. The molecular weight of ethanol is 46.069 g/mol.

The general mechanism of action is that the alcohol produces injury to cells by dehydration and precipitation of the cytoplasm or protoplasm. This accounts for its bactericidal and antifungal action.

The ethanol is a compound containing hydroxyl (OH^-) ions. OH^- ions saponify the lipids in the enveloping membrane, leading to destruction of the superficial structure [6]. This statement represents the correlation between the mechanism of action and the structure of ethanol. Correlation between the mechanism of action and the concentration can also be established. Namely, 70% ethanol was shown to be more effective antiseptic than 100% ethanol. This conclusion is based on the fact that ethanol causes coagulation of proteins on contact and accordingly the 100% ethanol when comes into contact with a microorganism creates hardened protein wall around the outside of the microorganism, rather than permating into its interior. Microorganisms can be very resilent, so the protein shell is rather to cause dormancy than death. This effect leads to revival of the microorganism and under the right circumstances, the cycle of reproduction will continue. When the concentration of the ethanol is 70%, the solution causes gradual coagulation, slowing down the microorganism from the inside out while penetrating.

When it comes to the antimicrobial spectrum, ethanol is highly effective against: mycoplasmas, gram–positive bacteria, gram–negative bacteria and pseudomonas; effective against: rickettsiae, enveloped viruses and acid–fast bacteria. Also, ethanol shows limited activity against chlamydiae and fungal spored, but shows no activity against: non-enveloped viruses, bacterial spored, coccidia and prions [7].

2.2 Povidone iodine

Povidone iodine is a stable chemical complex of polyvinylpyrrolidone (povidone, PVP) and elemental iodine. It contains from 9.0% to 12.0% available iodine, calculated on a dry basis. This unique complex was discovered in 1955 at the Industrial Toxicology Laboratories in Philadelphia by H. A. Shelanski and M. V. Shelanski. They carried out tests in vitro to demonstrate anti–bacterial activity, and found that the complex was less toxic in mice than tincture of iodine. Human clinical trials showed the product to be superior to other iodine formulations. Povidone iodine was immediately marketed, and has since become the universally preferred iodine antiseptic.

Povidone iodine structure is presented in Figure 2.

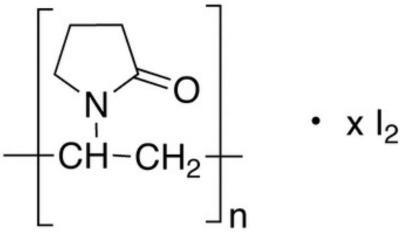

Figure 2. Chemical structure of povidone iodine

The molecular formula of this chemical complex is $C_6H_9I_2NO$. Povidone iodine appears ad yellowish - brown or reddish - brown, amorphous powder which is soluble in water and ethanol (96 per cent) and practically insoluble in acetone. The molecular weight is 364.953 g/mol.

Iodine acts by decreasing the oxygen requirements of aerobic microorganisms. Iodine interferes at the level of the respiratory chain of the microorganisms by blocking the transport of electrons through electrophilic reactions with the enzymes of the respiratory chain.

Iodine also interacts preferentially with the proteins of the cytoplasm membrane in a form with a positive (H_2O + I) or neutral (I_2 or HOI) charge [6]. This mechanism of action of iodine is correlated to its structure.

Also, the mechanism of action can be presented in relation to the concentration. Once the povidone-iodine complex reaches the cell wall, the free iodine released is rapidly cytotoxic, killing the prokaryotic cell within 10 seconds. Further free iodine is released from the povidone-iodine complex as free iodine is used up, until the available iodine is exhausted. The free iodine concentration has been shown to increase with more dilute concentrations of povidone-iodine, with a maximal free iodine concentration of 24 parts per million at 0.7%. The results show a significant difference in bactericidal activity in vivo between 5% and 1% povidone–iodine, with 5% povidone-iodine demonstrating more activity overall. Interestingly, there is no statistical difference between the two strengths with low initial bacterial loads - the difference becomes more markedonly as the initial load of bacteria increases. This is in contrast with results seen in vitro. In vivo, known inhibitors of povidone–iodine (blood, pus, fat, glove powder as well as protein containing solutions) may be present and may have a role of altering bactericidal efficacy, or the dose or volume of the povidone–iodine may vary depending on the contact time and retention within the conjunctival fornix [8].

Povidone iodine has wide antimicrobial spectrum. Namely, this chemical complex is highly effective against mycoplasmas and effective against: Gram positive bacteria, gram–negative bacteria, pseudomonads, rickettsiae, enveloped viruses, chlamydiae, fungal spores, acid-fast bacteria and bacterial spores. However, it shows limited activity against non–enveloped viruses and no activity against coccidia and prions [7].

2.3 Formaldehyde

Formaldehyde is a highly reactive aldehyde gas, but as a solution is used as a disinfectant (formalin) and is considered a hazardous compound and its vapor toxic.

Formaldehyde structure is shown in Figure 3.

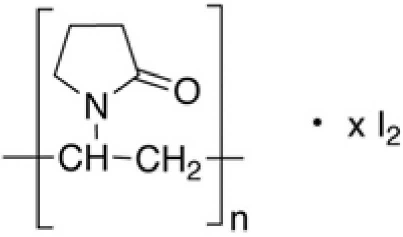

Figure 3. Chemical structure of formaldehyde

The molecular formula of this chemical compound is H_2CO or CH_2O. When it comes to the physicochemical properties, formaldehyde is a clear, colorless liquid which is miscible with water and with alcohol. It may be cloudy after storage. The molecular weight of formaldehyde is 30.026 g/mol.

The general mechanism of action of formaldehyde lies in its ability to produce insoluble complex compounds with proteins. Its mechanism of action is explained in *Streptomyces* spp. where formaldehyde catalyzes distinct carboxtpeptidation and transpeptidation reactions during the last stages of wall peptidoglycan synthesis. Mistaking a beta–lactam antibiotic molecule for normal substrate (i.e. a D-alanyl-D-alanine-terminated peptide), it becomes immobilized in the form of a long-lived, serine-ester-linked acyl enzyme and thus behave as penicillin-binding protein (PBP).

There is an established correlation between the mechanism of action and the structure of formaldehyde. Namely, this chemical compound acts on proteins by denaturation and on nucleic acids by alkylation, as follows:

$$O = CH_2 \leftrightarrow \text{Protein} - NH - CH_2 - OH$$
$$\rightarrow \text{Protein} - NH - CH_2 - NH - \text{Protein}$$

The reaction is irreversible at the level of nucleic acids:

$$O = CH_2 \rightarrow \text{Protein} - NH - CH_2 - NH - DNA$$

The action of formaldehyde is identical at the ribo– and deoxyribonucleotide levels, escept for guaniribo–deoxyribonucleotides. The 5' dGMP (deoxy-guanosine monophosphate) interacts more rapidly with formaldehyde than 5' GMP.

The reaction with receptive nucleotides occurs rapidly and the equilibrium shifts towards hydroxymethylation. This action is pH-dependent, working better at alkaline pH and less well at neutral or acid pH [6].

Formalin is a 37% solution of formaldehyde gas in water. Diluted to 5% formaldehyde it is an effective disinfectant; at 0.2% - 0.4% it can inactivate bacteria and viruses. This statement shows that there is correlation between the mechanism of action and the concentration in which this chemical compound is used.

When it comes to the antimicrobial spectrum, formaldehyde is highly effective against: mycoplasmas, Gram positive bacteria, Gram negative bacteria, pseudomonads, enveloped viruses; effective against: rickettsiae, chlamydiae, non–enveloped viruses, fungal spores, picornaviruses, parvoviruses, acid–fast bacteria, bacterial spores and it has no activity against coccidia and prions [7].

2.4 Hydrogen peroxide

Hydrogen peroxide is a strong oxidizing agent used in aqueous solution as a topical anti-infective. It is relatively unstable and solutions deteriorate over time unless stabilized by the addition of acetanilide or similar organic materials.

Hydrogen peroxide structure is presented in Figure 4.

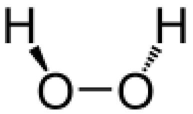

Figure 4. Chemical structure of hydrogen peroxide

The molecular formula of this chemical compound is H_2O_2. When it comes to the physicochemical properties, hydrogen peroxide is a colorless, clear liquid with a molecular weight of 34.014 g/mol.

The general mechanism of action at the cellular level can be explained by the ability of the hydrogen peroxide to induce DNA damage that appears to involve a role for transition metal ions bound to DNA, which may interact with H_2O_2 resulting in the production of a reactive radical species, most likely OH. This radical species found close to the DNA interacts with DNA forming purine and pyrimidine products characteristic of those found after the exposure of aqueous DNA solutions to ionizing radiation.

The pharmacologic activity of the drug depends on the release of nascent oxygen which has a powerful oxidizing effect that destroys some microorganisms and chemically alters many organic substances. When hydrogen peroxide topical solution comes in contact with tissues that contain the enzyme catalase, the solution releases oxygen which exerts antibacterial action; the mechanical effect of effervescence loosens tissue debris and pus. The release of nascent oxygen and effervescence is more rapid on wounds, denuded areas, and mucous membranes than on unbroken skin. The presence of reactive organic material such as pus and blood diminishes the efficiency of hydrogen peroxide. The antibacterial activity of hydrogen peroxide is relatively weak and slow and the drug exhibits poor tissue and wound penetration. Hydrogen peroxide's mechanical effect of effervescence and resultant removal of tissue debris is probably a more effective means of reducing the bacterial content of wounds, denuded areas, and mucous membranes than actual antibacterial activity. The drug also appears to have a styptic effect when applied topically to minot wounds. Concentrated solutions of hydrogen peroxide have a bleaching effect on hair and may injure tissue.

Also, peroxides play an important part in degrading the bacterial cell. In the presence of oxidising agents such as peroxides, bacteria such as *Escherichia coli* defend themselves by producing enzymes which either destroy the oxidising agent before bacterial degradation takes place or help the restoring mechanisms.

Oxidised molecules are more sensitive to proteolysis than other molecules, and it has been suggested that a 'system of cell senitisation' may enter into effect under the action of an oxidising agent such as H_2O_2 [6].

A correlation between the mechanism of action and the concentration of hydrogen peroxide can also be established. Hydrogen peroxide in the home is in dilluted form (3 - 10%) whereas industrial use involves concentrated solutions (30% or greater). Hydrogen peroxide (at a 5 - 20% concentration) is considered bactericidal, virucidal (non-enveloped viruses may be resistant), fungicidal and at high concentrations sporicidal. Its actovity against mycobacteria is limited [9].

When it comes to the antimicrobial spectrum, hydrogen peroxide is highly effective against mycoplasmas; effective against: Gram positive bacteria, Gram negative bacteria, pseudomonads, rickettsiae, enveloped viruses, chlamydiae, picornaviruses and bacterial spores. It has limited activity against: non-enveloped viruses, fungal spores, acid-fast bacteria and no activity against coccidia and prions [7].

3. Conclusions

- Infection control measures are important for the effective control, prevention and treatment of infection. Knowledge of emerging pathogens and resistance profile is essential for treatment against nosocomial infections.

- The structure and the activity of the antiseptic and the disinfectant are correlated. However, there is also a correlation between the concentration and the activity of the antiseptics and disinfectants. In conclusion, before choosing which antiseptic or disinfectant should be used, we must be familiar with its structure and in which concentration should be used in order to have the desired effect. On the contrary, it will not be possible to achieve the desired effect and it may be one of the reasons for the occurrence of intrahospital infections.

- Although, we need to mention that there is still not enough information available that could reflect the real situation about the correlation between the structure and the physicochemical properties of antiseptics and disinfectants with their activity.

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