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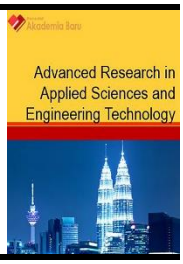

Biocide resistance

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ABSTRACT

The pandemic COVID-19 that the world are facing today has led to high usage of disinfectants and routinely used in the community. However, the extensive usage of biocides for disinfection could lead to antimicrobial resistance (AMR). Antimicrobial resistance has become the major caused that contributes increase in morbidity and mortality rate. The wide scale use of biocides creates selective stress that will favor bacteria in expressing resistance mechanisms and their dissemination. Some biocides have the potential to create cross resistance with the antibiotics and developing co-resistance to spread the Antimicrobial resistance (AMR). In this review, the author will discuss on the potential threat in the healthcare caused by the biocides that could drive the AMR to become worse.

Keywords:
Biocide resistance, antibiotic, sublethal concentration, efflux pump, cross resistance

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1. Introduction

Biocides is a chemical compound that capable in destroying or inhibiting the growth of microorganisms. Disinfectants, antiseptics and preservatives are examples of biocides that provide society with numerous benefits. They have important role in controlling bacteria growth in variety of applications, thus they must be managed wisely to prevent loss of activity overtime. It is paramount to prevent over usage of biocide in order to avoid the emergence of cross resistance and antimicrobial resistance. Apart from biocides, antibiotics also can help to kill bacteria by preventing infections in humans or animals.

There are cases reported regarding biocides resistance on low and high level of triclosan in S.aures, low level of quartenary compounds against P.aeruginosa. Also there is cases reported on provide resistance on isoniazid an antimicrobial agent. Study done by Puangseree et al.(2021) ,E.coli isolated from pigs, porks and pig carcass have develop resistance toward disinfectant and heavy metals such triclosan,benzalkonium chloride and chlorhexidine digluconate. Biocides can gives rise via mutation or by acquisition extrachromosomal genes. (Sheridan et al. (2014).Resistance specific on the classes

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of biocide and the likely and common for the biocide resistance to occur is due to changes in target cell permeability and biocide efflux. (Fraise , 2002)

Mechanism of bacteria become resistance to biocide can be due to target alteration in which biocides tends to act on one or multiple sites of the bacteria components such as cell wall, cell membrane or cytoplasm. (Poole , 2002)There is also data reported that bacteria cellular changes or impermeability may contribute in biocide resistance mostly in Gram Negative bacteria. Gigaouris et al. (2013) Changes involves in the surface outer hydrophobicity, outer membrane protein composition and outer membrane fatty acid composition. A review made by the International Scientific Forum on Home Hygiene (IFH) (2000) stated that the outer membrane of Gram-negative bacteria acts as a permeability barrier limit the penetration of hydrophobic molecules and the low fluidity of the Lipopolysachharide (LPS) leaflet slows down the inward diffusion of lipophilic compounds.

Efflux pump also can be paramount in bacteria resistance to biocide. Some bacteria become more tolerant to biocides by activating a system that “pumps out” toxic compounds. This reduces the efficacy of biocides. According to Slipski et al. (2020), bacteria associated with encoded Guanidinium-Selective Efflux Pump has higher resistance toward quartenary ammonium compound (QAC) disinfectants. Gram negative bacteria such Pseudomonas aeruginosa are also capable in removing disinfectant (eg QAC) or antibiotics by lacking of the lipid containing envelope preventing QACs from binding.(Hassan et al. (2010) and Delmar et al. (2014).80

2. Biocides resistance contribute to emergence of antibiotic resistance

Biocides in healthcare are widely used as disinfectants in preventing infections and decontaminating process of patient-care devices, environmental surfaces and intact skin. The usage of biocides on medical devices and devices are based on 3 level on inactivation: Low, Intermediate and High Level. There are few biocides that are capable in disinfecting at lower level. According to SCEINHR and European Commission 2009),Iodophor solution, Phenolic, Quaternary ammonium detergent solution are the biocide that able to disinfect by the concentration of dilution for use following the provided product label. While for Ethyl or isopropyl alcohol concentration at 70-90% is at the best killing effect. For intermediate level Phenolic and Sodium hyphochlorite belongs under this category.

The high level type of biocide was divided into Glutraldehyde with types of concentration :2% Glutaraldehyde and combination of 1.12% of Glutaraldehyde and 1.93% Phenol/Phenate.Followed by Hydrogen Peroxide with 3 types of concentration:7.35% of Hydrogen peroxide,7.35% Hydrogen Peroxide and paracetic acid (0.23%) and 1% Hydrogen peroxide and paracetic acid 0.08%.Ortho-phtalaldehyde with concentration 0.55% and Paracetic acid 0.2% also include under this category.(SCENIHR and European Comission, 2009)

All of the medical devices that penetrate sterile tissues and are heat sensitive will be disinfectant by using ethylene oxide or hydrogen plasma. Biocides also are used in disinfecting environmental surfaces such as near-patient surfaces (e.g. floors, walls, tables, bedrails, screens).However several issues has been reported due to the usage of biocides on environmental surfaces as it may contribute to epidemic or endemic spread of epidemiologically important bacteria, such as methicillin-resistant Staphylococcus aureus (MRSA) could survive on inanimate objects for a month (Kramer et al. (2006), vancomycin-resistant enterococci (VRE) and Clostridium difficile by acting as a reservoir from which health care workers contaminate their hands.(SCENIHR,2009).

Resistance towards quaternary ammonium compound (QACs) has been found in megaplasmid Psedumonas aeruginosa and Pseudomonas putida .It contain transposons with integrin genes coded for resistance.Sun et al. (2016).In 2003, there was an outbreak reported regarding QACs resistance organism in the healthcare industry. Moreover, 108 cases with 14 deathscytoges type 4b containing plasmid with resistance cassette bcrABC in a transposon that was resist and 4 cases of abortion was reported during an outbreak of listeriosis in the U.S. reported in 1998 to 1999 that is traced to a factory involving in manufacturing hotdog. This was caused by L. monoant to benzalkonium chloride.

A study done by Curio et al. (2015), found that resistance towards triclosan in E.coli and K.pneumonia was not only due to exposure triclosan itself but also due to other exposure of biocide compound such as benzalkonium chloride or ciprofloxacin .Besides that, triclosan resistance also found in a collection of 400 human and animal Salmonella enterica isolates in 4% and association with multiple resistance to a variety of other antibiotics in 56%.(Copitch et al. 2010). According to Stickler and Jones (2008) described that possibility of emergence of triclosan resistance in Proteus mirabilis associated with the urinary flora of catheterized patients.Suggestion for monitoring triclosan in clinical use in order to prevent urinary catheter encrustation and blockage.

For chlorhexidine, it has develop co resistance with develop resistance to antibiotics. The effect of reduced susceptibility to chlorhexidine are usually resistant to other antibiotics such as aminoglycoside and polymyxin. According to Ciusa et al. (2012), Acinetobacter baumannii strains with a reduced susceptibility to chlorhexidine a co-resistance to carbapenem, aminoglycoside, tetracyclin, and ciprofloxacin was found .11 of 120 chlorhexidine solutions were found in Trinidad to be contaminated with Pseudomonas spp., with resistance rates to ciprofloxacin of 58.3%, to norfloxacin of 50.0%, to tobramycin of 45.8%, and to gentamicin with 41.7% .Gajadhar et al. (2003). A stable resistance to chlorhexidine diacetate (CHA) was observed in strains of Pseudomonas stutzeri when exposed to gradually increasing concentration of antibacterial agent. (Tatawasart et al. (1999). According to Pereira et al. (2020), resistance of E.coli toward several biocides such as chlorhexidine, glutaraldehyde, benzalkonium chloride was observed and developing a cross resistant to at least one of the following antibiotic: ampicillin, chloramphenicol, and norfloxacin.

According to Chen et al. (2020), if concentration of biocides above the Minimum inhibitory concentration (MICs) or the Minimum bactericidal inhibition(MBCs) will have the killing effect toward the bacteria and will inhibit the resistance from develop. However the more important issue that one should also be aware would be the usage of inappropriate disinfectants that contain the sublethal levels of biocides.This will create resistance when expose to bacteria. As stated by Kampf (2018), antibiotic resistance may develop if sublethal concentrations of some biocidal agent being expose to various Gram-negative bacteria species.

3. Conclusion

Biocides resistance has the potential threat in developing cross resistance between antibiotics.The exposure bacteria to sublethal biocides will exacerbate the resistance. Further research need to be done to determine the biocide, their concentration that capable in generating antibiotic resistance. A monitoring programme in controlling the level of misuses of biocide should be develop for instance inadequate usage of cleaning products or inappropriate dilutions of disinfectants may lead to AMR. Enviromental studies in identifying and characterise development of resistance and cross-resistance to antibiotics following study on the misuse of biocide should be done in order to understand the impact of antimicrobial resistance on the epidemiology of resistant organism

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