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Review Article

BIOCIDE RESISTANCE: IS IT OFFERING MORE POTENCY TO THE SUPERBUGS ?

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ABSTRACT: The use of biocide chemicals is crucial for the elimination of microbial species required to prevent the spread of infectious diseases and ensure the safeguarding of animal and human health. Like antimicrobial drug resistance (AMR), anti-biocide resistance (ABR) may be a serious threat to healthcare, agriculture, animal husbandry, pisciculture as well as pharmaceutical and many other industries. Pathways of functioning of the antimicrobial drugs and biocides are alike in many cases, and among the patterns of resistance development in the microbes, such similarities are also found. Reaching such multi-drug and multi-biocide resistant microbes in the water bodies and other sectors of the environment may also cause serious effects on ecology, the environment, and the entire biosphere. Framing of strict legislative measures is required for the rational use of biocides by considering their spectrum of activity, effective concentration in different conditions, residue calculation, and after-use destruction. This review aims to explore the use, detection, and regulation of biocidal agents across different contexts, highlighting their application that can contribute to the concurrent development of biocidal resistance and overall antimicrobial resistance among microorganisms.

Keywords: Anti-biocide resistance, Antimicrobial resistance, Superbug, Healthcare, Ecology, Environment, Biosphere, Rational use.

INTRODUCTION

Antimicrobial resistance is now recognized as a major threat to public health and is considered to be the reason for the next global pandemic [1]. The emergence of resistance to antimicrobial agents likely began with the introduction of the first antimicrobial substance, penicillin, which was used to combat microorganisms [2]. Now, many study reports are available on multi-drug resistant organisms, even on the microorganisms resistant to almost all the available antimicrobial drugs [3]. In such a condition, it was thought that biocides could be effectively used to prevent surface colonization of the microorganisms and thus control their growth and multiplication. In that way, the initiation and spread of the diseases as well as the quantity of use of antimicrobial drugs could be minimized. In recent decades, the use of biocides has been promoted for cleaning and maintaining the sterility of environments in households, healthcare facilities, around patients, animal husbandry, and agriculture, to ensure hygienic and germ-free surroundings [4, 5].

BIOCIDES AND THEIR USE

Biocides are a single or a mixture of some antimicrobial substances having the ability to destroy or render the activities of the targeted microorganisms harmless by any means except the mechanical or physical one [6, 7]. They are commonly used in healthcare, domestic, and industry environments mainly for disinfection and other purposes to prevent microbial growth and contamination [8]. The term biocide covers disinfectants, sanitizers, antiseptics, sterilants, etc. The disinfectants are applied on the surface of any object or place to counter the microorganisms staying there. The antiseptics are applied to the body of any living entity for the same purpose. Sanitizers are used to sanitize (making germ-free) the hands and the sterilants are used to make some surfaces free of microorganisms [9, 10].

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Different biocides, mainly antiseptics and disinfectants are used at a large scale in healthcare and related purposes to control the spread of different diseases [11]. However the biocidal products are not at all outside the resistance development strategies of the microorganisms, and many microorganisms are identified as having the ability to resist different biocides [11].

COMMONLY USED BIOCIDES

The main biocides used in healthcare-related purposes and studied for their activities are alcohols, aldehyde-based compounds, peracetic acid, phenol, halogens, hydrogen peroxide, beta-propiolactone, chlorhexidine, quaternary ammonium compounds, weak organic acids, triclosan, chlorine releasing compounds, etc. [10, 11]. The most commonly used antiseptics are the mixture of chloroxylenol and terpineol, and the next place is held by Iodoform [9, 10,12].

Biocidal products are classified into 22 product types (PT) depending on their use. Although all these biocides can influence human health in different ways, the products categorized under Main Group 1 (PT 1 to PT 5) are mostly important in the development of resistance against them and their possible impact on the healthcare system [https://echa.europa.eu/regulations/biocidal-products-regulation/].

MECHANISM OF ACTION OF BIOCIDES

The use of different biocides is gaining more importance day by day due to the pressure of minimum use of antimicrobial therapeutic drugs for rapid development of resistance among different pathogenic organisms against them. To control the spread of organisms like methicillin-resistant *Staphylococcus aureus*, *Clostridioides difficile*, Avian Influenza virus, Covid 19 virus, etc. use of different biocides has increased rapidly in recent years. In many cases, they affect all vegetative microbes that come in contact with them, without considering their actual pathogenicity. Although the complete mechanisms of action for every biocide are still not fully understood, substantial progress has been made in characterizing their effects. Biocides generally show their activities by influencing different parts of the microbial cells like cell envelope permeability, efflux mechanisms, and surface property, as well as bypassing metabolic blockage of the microbes, etc. The cytoplasmic membrane of the organisms is mostly targeted; then their enzymes other proteins and the nucleic acids of the microbes are targeted by the least number of the biocides. Generally, the bacterial spores are not affected by the biocides. Biocides generally act on multiple targets of the organisms. Incurring damage of the number of microbial cell targets and the ultimate effect as total killing (cidal effect) or controlling the growth (static effect) varies between biocides and the type of the affected organisms [12,13].

DEVELOPMENT AND EXPRESSION OF BIOCIDE RESISTANCE

Like all other chemicals having antimicrobial activities, every biocide has a specific range of organisms on which they can show their detrimental effects. Biocides are to be used in some specific dose and should be in physical touch with the organisms for a minimum time to show their activities. The vegetative forms of the susceptible organisms, both pathogenic and non-pathogenic, are the common targets of the biocides. Generally, spores of the organisms and the organisms stay inside any protective shield like slimy materials, sputum, bacterial biofilms, etc. can bypass the effect of biocide, partially or completely [14,15,16].

Like antimicrobial resistance, anti-biocidal resistance may also be intrinsic, acquired by mutation of genes or via horizontal gene transfer. Among the intrinsic mechanisms followed, modification of the structure of the cell membrane, development of specific efflux pumps in the microbial cell, and formation of biofilm or endospores are important [4].

Among different biocides, the tendency of development of resistance is found different. Hydrogen peroxide, alcohols, and weak organic acids are very much impervious to the development of microbial resistance against them. The aldehyde group of chemicals and the chlorine-realizing chemicals also have good resistance against that trend. However, resistance development against quaternary ammonium compounds (QAC), chlorhexidine, etc is comparatively common and resistance development against chemicals like triclosan is found very common among the different microbial populations. Biocide resistance against yeast, *Mycobacterium*, and many Gram-positive and Gram-negative bacteria are already reported [11]. Like the difference in susceptibility towards antimicrobial drugs, the differences in the tendency to develop resistance against biocides also differ among microorganisms. Many Gram-negative bacteria (such as *E. coli*, *Pseudomonas* sp., *Proteus* sp., *Klebsiella* sp., etc.) are less permeable to many biocides due to the presence of lipopolysaccharide membranes of their cell envelope [4].

Biocidal resistance and antimicrobial resistance

The emergence of biocide resistance among various microorganisms and its potential effects on the total healthcare system is perhaps not given proper attention. The mechanisms identified in different biocide resistances are found to have very close similarities with the mechanisms followed by the microorganisms to resist different anti-microbial substances [17]. So, there may be cross-resistance development (resistance towards biocide can also give an organism the resistance power towards one/ a few/ many antimicrobial substances) and ample study is required to find sufficient evidence in this regard [18, 19].

It is assumed that the development of anti-microbial resistance (AMR) among the microorganisms may have the original base on biocide resistance in many cases. The selection pressure imposed by the biocides can lead to the creation of biocide-resistant microorganisms, which may have serious impacts on the development of antimicrobial resistance to various antimicrobial substances including antibiotics [20].

The entire procedure may have some far more serious implications in the resistance development among the microorganisms causing nosocomial infections, as different biocides are routinely used in almost all the places and sources of microorganisms causing nosocomial infections [18].

Many deaths are reported, especially in developing countries, from the infection of multi-drug resistant (MDR) microorganisms with moderate virulence, as some opportunistic pathogens, in the intensive care units (ICU) of the hospitals [5]. Among them, the ESKAPE group of organisms (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species) are considered the most common bacteria [4, 21]. The development of resistance against antibiotics as well as different biocides by such organisms are becoming a threat to human civilization [1, 3]. Biocide resistance developed by the bacteria is discussed here, but such resistances are also documented in different fungi and viruses [4].

The platform of anti-biocide resistance development

It is a common practice to use biocides in such a manner that they ultimately reach the wastewater and different water bodies. Due to serial dilutions, the concentration of biocides becomes very low in the wastewater and other environmental exposures. That led to the development of resistance against the biocides by the organisms staying in the environment thus leading to the survival of the resistant bacteria selectively [13, 14].

So, either the inappropriate use of a biocide, or the reaching of biocides to the microbes at a lower (below the killing) concentration can assist the microorganisms to develop resistance against the biocides. On the other hand, biocides can also assist the promotion of antimicrobial resistance genes from one organism to another [8,12,14].

The main features of the development of biocide resistance can be listed below.

1. The resistance of the microbes towards biocides may be inherent or intrinsic. The non-susceptible organisms that become unaffected by a biocide generally do not permit the biocide/s to enter their cells.
2. Among the microorganisms with acquired resistance towards biocides, mutation of the preexisting genetic materials or uptake of the genetic materials (plasmid-borne) by horizontally transfer genes may be the actual reason for working from behind.
3. Anti-biocide resistance developed in any nonpathogenic organism can be transferred to any pathogenic organism to convert that into some pathogenic, biocide-resistant one.
4. Some bacteria can modify their external cellular envelope to resist the biocides entering the cell and thus keep the concentration of the biocides inside their cells at a very minimum level to stay (permeability modification).
5. Different target sites of the biocides are altered by the same microbes to avoid the detrimental effects of the biocide molecules.
6. Some microorganisms pump out the biocides outside their cells (efflux pump).
7. Some bacteria use their cellular enzymes to modify the biocides entered inside the cells to some harmless material.
8. The development of power to produce biofilms is the way followed by some microbes to resist reaching the biocides to their cell envelope [4, 23, 24].

A detailed summary of frequently employed biocides is provided in Table 1, encompassing their main uses, mechanisms of action, and susceptibility to resistance development.

Exchange of resistance

There are possibilities for the exchange of resistance against antibiotics and biocides among the microorganisms [4, 12]. Co-resistance and cross-resistance towards both types of antimicrobial materials are also documented [15, 18, 19]. There are also possibilities of influence of the development of resistance against biocides by the antibiotics and vice versa [13, 22, 23].

Effect of biocide resistance on the development of antimicrobial resistance and vice versa

Scientific evidence from laboratory investigations has established a link between biocide usage and the development of antibiotic resistance in bacteria. This phenomenon is not confirmed in the field condition due to lack of authentic data. Biocide exposure can create selection pressure and the surviving bacteria with resistant genes to the biocides can transfer such genes to other bacteria leading them to develop resistance against the biocides. When such a resistance gene can reach any AMR organisms, it may make such organisms resistant to both antibiotics and other antimicrobial drugs as well as the biocide/s [4, 12, 14].

According to the available data and research reports, a correlation has been observed between the use of certain biocides and the development of resistance against some antibiotics. The use of quaternary ammonium compounds, chlorhexidine, and triclosan are strongly related to cross-resistance development to some other antibiotics like vancomycin, tetracyclines, chloramphenicol, imipenem, ciprofloxacin and colistin [8, 11, 13].

It was observed in some experiments that among the biocide-resistant strains of bacteria, a very good portion also developed resistance against many antibiotics. The bacteria developed biocide resistance was also found to increase their capacity for biofilm formation in some cases [19].

Many serious issues are coming out along with the identification of resistant strains of bacteria against different disinfectants and other biocide materials. They can influence the transmission of different diseases through fomites and other means, can influence food production as well, and can create serious problems in the processing of different medical devices and the production of pharmaceutical drugs that require a sterile environment during their production and packaging [4, 19].

A reverse tendency was also pointed out. The multidrug-resistant (MDR) bacterial isolate was found to have reduced susceptibility toward commonly used biocides. Such biocide resistance development when happened among the MDR bacteria causing nosocomial infections (*S. aureus*, *P. auriginosa*, *E. coli*, *K. pneumonia*, etc.), and the entire modern healthcare system come under a strong threat to its efficacy in the future [16, 18].

Possible reasons for biocide residence development

It has already been noticed that behind the development of AMR against biocides at an accelerated speed in recent times, uncontrolled use and misuse of biocides play the deciding roles by influencing various other factors [4, 14]. The possible reasons working behind biocide resistance development can be listed as below.

1. Unrestricted use of some biocides

Many commonly used biocides, especially antiseptics, disinfectants, cleansing agents, sanitizers, sterilizing agents, and preservatives are used in some uncontrolled way. There is even no legislative pressure on their use. Common people use these materials as per their own decision - with or without any knowledge about their use and aftereffects. Such attitude is leading to easy development of resistance among the microorganisms against biocides like antibiotics.

2. Wrong selection of biocides

Knowledge about the use of the spectrum of efficacy of each biocide is very important. Periodical change of biocide is required in the places of their regular use (as in the toilets of the health centers, railway stations, etc.). This point is not given proper importance.

3. Wrong dilution of biocides

People have a common tendency to dilute biocides as per their assumptions. It may be dangerous, as low concentrations of the biocides invite easy resistance development against them.

4. Lesser time attachment with the microbes

Every biocide requires minimum time attachment with the susceptible microorganisms to neutralize them. Lesser time attachment leads to easy resistance development.

5. Use on uncleaned materials or surfaces.

When microbes are mixed with other materials, they can protect themselves from the effects of the biocides. In such cases, either mixing of the whole materials with the biocides or use of some higher dose is required to make them susceptible to the biocides.

6. Residual level of biocides after completion of the work

The residual concentration of the biocides in the used materials, fomites, as well as the area of their use, is very important. The target should be there for zero residual status of the materials on which they were used. The area should be cleaned properly to prevent the environmental organisms from coming in contact with the residual biocides.

7. Easy access to water bodies and other places for easy exposure to the environment

After the use of the biocides, proper washing and disposal of the used materials are necessary. It is generally washed to flow them towards the water bodies like canals, rivers, ponds, etc. All such tendencies can cause easy development of anti-biocide resistance among the microbes [4, 8, 19].

IMPACTS OF BIOCIDE RESISTANCE ON HEALTH

The development of resistance against antibiotics, biocides, and other antimicrobial agents is an outcome of the microorganisms' struggle for their existence. The irrational and unnecessary use of these substances just increases the chance and speed of development of such résistance [25].

Some serious impacts of the biocide resistance have been identified or assumed in different fields like healthcare, food industries, agriculture, horticulture, animal husbandry, fishery science, etc., but detailed study reports related to such effects are not available. These effects are interlinked in many cases and ultimately show their effects on human health [26, 27].

Effect of development of biocide resistance among the microorganisms, their cross-resistance and co-resistances with antimicrobial drug resistance can induce many serious impacts on healthcare practices. There is a possibility of the development of some disease microbes with resistance against many/most of the biocides and antimicrobial drugs together. This may render all or most of the biocides, antibiotics, and other antimicrobial drugs ineffective against them [12]. Such a condition will drastically influence many very important sectors like the following.

1. Control the nosocomial infections caused by organisms of the ESKAPE group as well as other microorganisms [8],

2. Control the growth of different microbes in the fomites used for different purposes in health centers, places of human gathering (like railway stations, airports, transport vehicles, etc.), and their spread afterward,

3. Creation of germ-free environment in the operation theatre, intensive care unit, dialysis unit, etc. areas of important healthcare facilities,

4. Control of microbes and pests in the field of agriculture,

5. Control of diseases among animals and fishes in animal husbandry and pisciculture practices,

6. The spread of resistant microbes affecting the huge number of organisms living in marine environments,

7. Creation of germ-free environment for different food processing industries (meat processing, fruit processing, etc.),

8. Creation of an environment with a minimum microbial population is required in many other industries including the Pharma industries, etc. [21, 26, 27].

9. Control of zoonotic diseases, as many pathogens (*E. coli*, *Vibrio* sp., *Streptococcus* sp., *Salmonella* sp., *Listeria* sp., *Clostridium* sp., *Campylobacter* sp., *Aspergillus* sp., *Candida* sp., *Cryptococcus* sp., etc.) are capable to cause diseases among human coming from contaminated food or animal contact and currently categorized under AMR group.

10. Effect on fertility of soil and impact on biodiversity and ecological status after reaching the water bodies - as reaching of biocides and availability of biocide resistance gene to the microbes present in these areas can impact different chains of the biosphere. Entire biotic lives may be influenced and can ultimately bring severe detrimental effects on the environment and health [4].

FUTURE PERSPECTIVE

Considering the history of the development of multidrug-resistant bacteria, the Superbug, some precautionary measures have to be taken during the use of the biocides.

1. The development of resistance against the biocides may lead to the development of cross-resistance to unrelated antimicrobial drugs including antibiotics by different microorganisms [12]. So, proper importance on that subject is to be given and proper study as well as field reporting and then proper analysis of these data is required to understand the seriousness of the problem.

2. There may be some detailed regulations and standardized protocols for the effective and strict use

Table 1. Development of resistance against some biocides by the microorganisms.

Category	Example	Use/ Active against	Mechanism of action	Resistance mechanism developed by microbes
Quaternary Ammonium Compounds (QACs)	Benzalkonium chloride (BAC),Cetylpyridinum chloride (CPC) Alkyltrimethylammonium bromide (cetrimide) [14, 21].	Active against bacteria, fungus, enveloped viruses, and parasites. Used mainly for disinfection [14, 21].	QACs are cationic surfactants. After adsorption to the cell and reaching the cell membrane, these cause the release of the cellular components outside through the disrupted cellular membrane leading to cell death [14, 21].	Formation of biofilms (as seen in *P. aeruginosa*) [14].
Chlorine-Releasing Agents (CRA)	Sodium hypochlorite (NaOCl), Hypochlorous acid (HOCl), Sodium dichloroisocyanurate [14].	Chlorine gas, sodium hypochlorite, and calcium hypochlorite are used in water treatment. Commonly used in sanitation and disinfection in hospital, industrial, and household settings. Sodium dichloro isocyanurate in industry, HOCl in household materials like mouthwashes; also used as/in clinical disinfectants, sanitizers, wound care, and podiatry [6, 14, 21].	Sporicidal, bactericidal, mycobactericidal, fungicidal, active against enveloped viruses. These are strong oxidizing agents that can irreversibly damage the microbes by acting on DNA and protein synthesis and can destroy cell membrane permeability and transport [6, 14].	Formation of biofilms in HOCl exposure among Gram-negative bacteria through overproduction of extracellular polymeric substances (EPS). Few reports of low-level cross-resistance are available to some other antimicrobials after exposure to low concentrations of sodium hypochlorite [6, 14].
Biguanides	Chlorhexidine digluconate (CHG), Polyhexamethylene biguanides (PHMB) [14].	Active against non-speculating bacteria and yeasts. Used as a safe antiseptic with low toxicity, to maintain the hygiene of the hand and oral cavity, as a disinfectant in healthcare instruments, wound treatment, etc. [6, 14].	The compounds act as an attraction of the negatively charged bacterial cell, then uptake of the compound happens that attack the cytoplasmic membrane of the cell causing inhibition of the membrane-bound enzymes along with leakage of intracellular materials. Chlorhexidine can cause precipitation of cytoplasm and coagulation and precipitation of intracellular constituents such as proteins and nucleic acids at high concentrations [6, 21].	Changing of cell membrane charge attraction and use of efflux pumps are documented. Cross-resistance to other microbes is also assumed [6, 14].
Peroxy-acetic acid (also known as peracetic acid or PAA)	Peracetic acid is obtained by reacting hydrogen peroxide with acetic acid in an aqueous solution [6, 14].	Bactericidal, sporicidal, virucidal, and fungicidal; are used as liquid sterilent of medical devices and as surface sterilent [6].	It acts as an oxidizing agent and works by denaturing proteins and enzymes of the cell and by oxidizing sulfhydryl bonds, can increase cell wall permeability [6, 7].	Reports of resistance development by the microbes in biofilm is available [6, 21].
Hydrogen Peroxide	Used at liquid and vapor form [6, 14].	Active against bacteria, spores, yeasts, and viruses. Used for the disinfection of skin, hospital items, and hard surfaces in healthcare and veterinary institutions; in food industries; also used as an antiseptic and sterilizing agent [6, 14, 21].	Oxidizing agents; act on extracellular and intracellular targets; the main mechanisms identified are incurring induced membrane damage, damage of membrane lipids, intracellular protein, ribosomes, enzymes, and DNA. It is proposed that exposed sulfhydryl groups and double bonds are particularly targeted [6, 14, 21].	Reports of resistance development by *S. cerevisiae*, *E. coli, Mycobacterium tuberculosis,* and *Campylobacter jejuni* are available [6, 14, 21]

Category	Example	Use/ Active against	Mechanism of action	Resistance mechanism developed by microbes
Lactic acid and other weak organic acids	Acetic acid (vinegar), lactic acid [6, 7].	Preservation of food; to decontaminate infected environment as well as the meat carcasses in the food industry [6, 7].	Possibly work by membrane perturbations. Accumulation of anions inside the cell cytoplasm leads to osmotic stress and obstruction of the enzymatic and metabolic functions [6, 7].	Some reports of resistance development among *E. coli*, *S. aureus, S.* Typhimurium*, L. monocytogenes,* and *C. jejuni* are available [6, 7].
Triclosan	It is a chlorinated biphenyl [6, 21]	Active against bacteria and yeast; widely used in different household products including antimicrobial soaps, cosmetics, etc. [6, 21]	By acting on enoyl-acyl carrier protein reductase, it inhibits fatty acid biosynthesis by acting on enoyl-acyl carrier protein reductase (ENR) [6, 21].	After exposure to that biocide, bacterial isolates may develop cross-resistance to antibiotics and other biocidal products. Skin absorption may lead to resistance and cross-resistance development in the human body due to changes in the microbiome population and size. Modification of ENR, upregulation of efflux pumps, etc. are identified [6, 21].

of biocides in particular fields and purposes. Excess or low-level use of the biocides should be prohibited.

3. Parameters like dilution, effective concentration like Minimum Inhibitory Concentration (MIC) (like the actual reaching concentration of the microbes staying inside the biofilms), etc. are to be determined and followed strictly during the use of the biocides [11, 28].

4. There should be a proper disposal plan for the biocides after their work has been completed.

5. In no cases, biocides should be allowed to mix with the wastewater and/or to reach the water bodies and other places to affect the ecology and environment.

6. The residue level of the biocides on the materials and surroundings should be checked after completion of the purpose of their use (as biocide residue is found in medical devices and implants) and it must be kept under a permissible limit [22, 26, 27].

7. Some alternatives to presently used chemical biocides are already identified and their efficacy study has been performed on a limited scale. Different active compounds isolated from plant or animal origin [22, 29], vegetable oils [30, 31, 32], diluent extracts of different dry plant parts, etc. [33] are reported in this regard. However, as per some reports, succulent extracts or latex of some plants can be used directly as some effective biocides [34].

CONCLUSION

The emergence of biocide resistance poses a substantial threat alone as well as for its connection to the development of anti-microbial drug resistance (AMR) in microorganisms. In many cases, similar pathways are followed by the organisms to develop resistance against materials of these two categories. There is evidence of the influence of AMR by the anti-biocide resistance and the reverse phenomenon is also documented. The selection pressure created by the biocides and the diluted biocides can not only invite resistance against them but also inspire resistance development against the antimicrobial drugs by the microorganisms. Reaching of biocides and their resistant genes in the environment through water and fomites can cause a serious detrimental impact on soil fertility, ecosystem, and biodiversity, apart from the direct impact on health and industries. Various alternatives of presently used chemical biocides having positive study reports are to be studied in detail. The plant-derived biocides including the essential oils, diluents' extracts, isolated compounds of the plants as well as the pressure extract or latex are to be studied to get the multi-component biocides possibly having a far lesser chance of development of resistance for combined multiple ways of activities of them.

REFERENCES

1. Tiwaskar M, Vora A, Saraf A, Bhadade R, Choudhari S, *et al.* Defeating the silent enemy: antimicrobial resistance looming as the next global pandemic. J Assoc Physicians India. 2024; 72(3):66-72.

2. Hunt D, Kates OS. A brief history of antimicrobial resistance. AMA J Ethics. 2024; 26(5):E408-417, DOI:10.1001/amajethics.2024.408.

3. Pattanayak, S. Alternative to antibiotics from herbal origin-outline of a comprehensive research project. Curr

Pharmacogenomics Person Med. 2018; 16:09-62, DOI:10.2174/1875692116666180419154033.

4. Meade E, Slatter MA, Garvey M. Biocidal resistance in clinically relevant microbial species: A major public health risk. Pathogens. 2021; 10:598, DOI:10.3390/pathogens10050598.

5. Teng J, Imani S, Zhou A, Zhao Y, Du L, *et al.* Combatting resistance: Understanding multi-drug resistant pathogens in intensive care units. Biomedici Pharmacotherap. 2023; 167:115564, DOI:10.1016/j.biopha.2023.115564.

6. Heger W, Hahn S, Schneider K, Gartiser S, Mangelsdorf I, *et. al.* Exposure to biocides from articles of daily use. Chirurgische Praxis. 2008; 68(4):755-764.

7. Hahn S, Schneider K, Gartiser S, Heger W, Mangelsdorf I. Consumer exposure to biocides - identification of relevant sources and evaluation of possible health effects. Environ Health. 2010; 9:7, DOI:10.1186/1476-069X-9-7.

8. Jones IA, Joshi LT. Biocide use in the antimicrobial era: A review. Molecules. 2021; 26:2276. DOI:10.3390/molecules26082276.

9. McDonnell G, Russell AD. Antiseptics and disinfectants: activity, action, and resistance. Clin Microbiol Rev. 1999; 12(1):147-179, DOI:10.1128/CMR.12.1.147.

10. Disinfection 101. 2023; The center Food security and Public Health, College of Veterinary Medicine, Lowa State University, www.cfsph.iastate.edu/Disinfection/Assets/Disinfection101.pdf.

11. Collet JF, Delhaye A, Leverrier P. Literature review on the development of (cross-) resistances to antimicrobials following the use of biocidal products. 2022; Louvain and Brussels: De Duve Institute/FPS Public Health, Food Chain Safety and Environment.

12. Maillard J-Y. Resistance of bacteria to biocides. Microbiol Spectr. 2018; 6(2), DOI:10.1128/microbiolspec.ARBA-0006-2017.

13. Goudarzi M. Navidinia M. Overview perspective of bacterial strategies of resistance to biocides and antibiotics. Arch Clin Infect Dis. 2019; 14(2), DOI:10.5812/archcid.65744.

14. SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks). Effects of Biocides on antibiotic resistance, Assessment of the Antibiotic Resistance Effects of Biocides. 2009.

15. Maillard, JY, Pascoe M. Disinfectants and antiseptics: mechanisms of action and resistance. Nat Rev Microbiol. 2024; 22(1):4-17, DOI:10.1038/s41579-023-00958-3.

16. Samanta I, Bandyopadhyay S. Cross-resistance between biocides and antimicrobials, In: Antimicrobial Resistance in Agriculture, Academic Press, 2020; 28:327-333, DOI:10.1016/B978-0-12-815770-1.00028-6.

17. Coombs K, Rodriguez-Quijada C, Clevenger JO, Sauer-Budge AF. Current understanding of potential linkages between biocide tolerance and antibiotic cross-resistance. Microorganisms. 2023; 11(8):2000. DOI:10.3390/microorganisms11082000.

18. Gupta P, Bhatia M, Gupta P, Omar BJ. Emerging biocide resistance among multidrug-resistant bacteria: myth or reality? A pilot study. Pharm Bioallied Sci. 2018; 10(2):96-101, DOI:10.4103/JPBS.JPBS_24_18.

19. Pereira BMP, Wang X, Tagkopoulos I. Biocide-induced emergence of antibiotic resistance in *Escherichia coli*. Front Microbiol. 2021; 12:640923. DOI:10.3389/fmicb.2021.640923.

20. Kampf G. Antibiotic resistance can be enhanced in gram-positive species by some biocidal agents used for disinfection. Antibiotics. 2019; 8(1):13, DOI:10.3390/antibiotics8010013.

21. De Oliveira DMP, Forde BM, Kidd TJ, Harris PNA, Schembri MA, *et al.* Antimicrobial resistance in ESKAPE pathogens. Clin Microbiol Rev. 2020; 33(3):e00181-19, DOI:10.1128/cmr.00181-19.

22. Elekhnawy E, Sonbol F, Abdelaziz A, Elbanna T. Potential impact of biocide adaptation on selection of antibiotic resistance in bacterial isolates. . Future J Pharmaceut Sci. 2020; 6:97, DOI:10.1186/s43094-020-00119-w.

23. Chieffi D, Fanelli F, Fusco V. Antimicrobial and biocide resistance in *Staphylococcus aureus* : genomic features, decontamination strategies, and the role of *S. aureus* complex-related species, with a focus on ready-to-eat food and food-contact surfaces. Front Food Sci Technol. 2023; 3:1165871, DOI:10.3389/frfst.2023.1165871.

24. Vijayakumar R, Sandle T. A review on biocide reduced susceptibility due to plasmid borne antiseptic-resistant genes-special notes on pharmaceutical environmental isolates. J Applied Microbiol. 2018; 126:1011-1022.

25. Pattanayak S. Alternative to antibiotics - preparation for post antibiotic era. Explor Anim Med Res. 2017; 7(1):05-10.

26. FAO (Food and Agriculture Organization of the United Nations). Biocides and Antimicrobial Resistance Summary Report of an FAO Meeting of Experts. FAO Antimicrobial Resistance Working Group. 2018; https://openknowledge.fao.org/server/api/core/bitstreams/b5d3fd50-b43a-42e1-89b9-f658ef4fda41/content.

27. Miller SA, Ferreira JP, LeJeune JT. Antimicrobial use and resistance in plant agriculture: A one health perspective. Agriculture. 2022; 12(2):289, DOI:10.3390/agriculture12020289.

28. Murray LM, Hayes A, Snape J, Kasprzyk-Hordern B, Gaze WH, Murray AK. Co-selection for antibiotic resistance by environmental contaminants. npj Antimicrob Resist. 2024; 2:9, DOI:10.1038/s44259-024-00026-7.

29. Pawlowska A, Stepczynska M. Natural biocidal compounds of plant origin as biodegradable materials modifiers. J Polym Environ. 2022; 30(5):1683-1708, DOI:10.1007/s10924-021-02315-y.

30. Argyri AA, Doulgeraki AI, Varla EG, Bikouli VC, Natskoulis PI, *et al.* Evaluation of plant origin essential oils as herbal biocides for the protection of caves belonging to natural and cultural heritage sites. Microorganisms. 2021; 9(9):1836, DOI:10.3390/microorganisms9091836.

31. Onyamoche EP. The importance of using natural product compounds as an alternative to chemically based disinfectants and germicides. Biomed J Sci Tech Res. 2023; 51(3), DOI:10.26717/BJSTR.2023.51.008098.

32. Marco A, Santos S, Caetano J, Pintado M, Vieira E, Moreira PR. Basil essential oil as an alternative to commercial biocides against fungi associated with black stains in mural painting, Building Environment. 2020; 167:106459, DOI:10.1016/j.buildenv.2019.106459.

33. Zain WSM, Salleh NIH, Abdullah A. Natural biocides for mitigation of sulphate reducing bacteria. Internati J Corrosion. 2018; DOI:10.1155/2018/3567569.

34. Pattanayak S. Antimicrobial formulation. Patent application no. 1367/KOL/2014, Journal no. 32/2016 of Controller general of patients, designs and trademarks, Govt. of India. DOI:10.13140/RG.2.2.20106.54729.

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