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Antiseptics and Disinfectants: Activity, Action, and Resistance

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ABSTRACT

Antiseptics and disinfectants are extensively used in hospitals and other health care settings for a variety of topical and hard-surface applications. A wide variety of active chemical agents (biocides) are found in these products, many of which have been used for hundreds of years, including alcohols, phenols, iodine, and chlorine. Most of these active agents demonstrate broad-spectrum antimicrobial activity; however, little is known about the mode of action of these agents in comparison to antibiotics. This review considers what is known about the mode of action and spectrum of activity of antiseptics and disinfectants. The widespread use of these products has prompted some speculation on the development of microbial resistance, in particular whether antibiotic resistance is induced by antiseptics or disinfectants. Known mechanisms of microbial resistance (both intrinsic and acquired) to biocides are reviewed, with emphasis on the clinical implications of these reports.

Keywords:

INTRODUCTION

Antiseptics and disinfectants are used extensively in hospitals and other health care settings for a variety of topical and hard-surface applications. In particular, they are an essential part of infection control practices and aid in the prevention of nosocomial infections. Mounting concerns over the potential for microbial contamination and infection risks in the food and general consumer markets have also led to increased use of antiseptics and disinfectants by the general public. A wide variety of active chemical agents (or "biocides") are found in these products, many of which have been used for hundreds of years for antisepsis, disinfection, and preservation. Despite this, less is known about the mode of action of these active agents than about antibiotics. In general, biocides have a broader spectrum of activity than antibiotics, and, while antibiotics tend to have specific intracellular targets, biocides may have multiple targets. The widespread use of antiseptic and disinfectant products has prompted some speculation on the development of microbial resistance, in particular cross-resistance to antibiotics. This review considers what is known about the mode of action of, and mechanisms of microbial resistance to, antiseptics and disinfectants and attempts, wherever possible, to relate current knowledge to the clinical environment.

It is important to note that many of these biocides may be used singly or in combination in a variety of products which vary considerably in activity against microorganisms. Antimicrobial activity can be influenced by many factors such as formulation

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effects, presence of an organic load, synergy, temperature, dilution, and test method. These issues are beyond the scope of this review and are discussed elsewhere.

DEFINITIONS

"Biocide" is a general term describing a chemical agent, usually broad spectrum, that inactivates microorganisms. Because biocides range in antimicrobial activity, other terms may be more specific, including "-static," referring to agents which inhibit growth (e.g., bacteriostatic, fungistatic, and sporistatic) and "-cidal," referring to agents which kill the target organism (e.g., sporicidal, virucidal, and bactericidal). For the purpose of this review, antibiotics are defined as naturally occurring or synthetic organic substances which inhibit or destroy selective bacteria or other microorganisms, generally at low concentrations; antiseptics are biocides or products that destroy or inhibit the growth of microorganisms in or on living tissue (e.g. health care personnel handwashes and surgical scrubs); and disinfectants are similar but generally are products or biocides that are used on inanimate objects or surfaces. Disinfectants can be sporostatic but are not necessarily sporicidal.

Sterilization refers to a physical or chemical process that completely destroys or removes all microbial life, including spores. Preservation is the prevention of multiplication of microorganisms in formulated products, including pharmaceuticals and foods. A number of biocides are also used for cleaning purposes; cleaning in these cases refers to the physical removal of foreign material from a surface.

MECHANISMS OF ACTION

Considerable progress has been made in understanding the mechanisms of the antibacterial action of antiseptics and disinfectants. By contrast, studies on their modes of action against fungi viruses and protozoa have been rather sparse. Furthermore, little is known about the means whereby these agents inactivate prions.

Whatever the type of microbial cell (or entity), it is probable that there is a common sequence of events. This can be envisaged as interaction of the antiseptic or disinfectant with the cell surface followed by penetration into the cell and action at the target site(s). The nature and composition of the surface vary from one cell type (or entity) to another but can also alter as a result of changes in the environment (Interaction at the cell surface can produce a significant effect on viability (e.g. with glutaraldehyde) but most antimicrobial agents appear to be active intracellularly (The outermost layers of microbial cells can thus have a significant effect on their susceptibility (or insusceptibility) to antiseptics and disinfectants; it is disappointing how little is known about the passage of these antimicrobial agents into different types of microorganisms. Potentiation of activity of most biocides may be achieved by the use of various additives, as shown in later parts of this review.

In this section, the mechanisms of antimicrobial action of a range of chemical agents that are used as antiseptics or disinfectants or both are discussed. Different types of microorganisms are considered, and similarities or differences in the nature of the effect are emphasized.

Summary of mechanisms of antibacterial action of antiseptics and disinfectants

General Methodology: A battery of techniques areavailable for studying the mechanisms of action of antiseptics and disinfectants on microorganisms, especially bacteria. These include examination of uptake (lysis and leakage of intracellular constituents, perturbation of cell homeostasis effects on model membranes inhibition of enzymes, electron transport, and oxidative phosphorylation interaction with macromolecules effects on macromolecular biosynthetic processes (and microscopic examination of biocide-exposed cells Additional and useful information can be obtained by calculating concentration exponents (n values and relating these to membrane activity Many of these procedures are valuable for detecting and evaluating antiseptics or disinfectants used in combination.

Similar techniques have been used to study the activity of antiseptics and disinfectants against fungi, in particular yeasts. Additionally, studies on cell wall porosity may provide useful information about intracellular entry of disinfectants and antiseptics Mechanisms of antiprotozoal action have not been widely investigated. One reason for this is the difficulty in culturing some protozoa (e.g.,Cryptosporidium) under laboratory conditions. However, the different life stages (trophozoites and cysts) do provide a fascinating example of the problem of how changes in cytology and physiology can modify responses to antiseptics and disinfectants. Khunkitti et al. have explored this aspect by using indices of viability, leakage, uptake, and electron microscopy as experimental tools.

Some of these procedures can also be modified for studying effects on viruses and phages (e.g., uptake to whole cells and viral or phage components, effects on nucleic acids and proteins, and electron microscopy) (Viral targets are predominantly the viral envelope (if present), derived from the host cell cytoplasmic or nuclear membrane; the capsid, which is responsible for the shape of virus particles and for the protection of viral nucleic acid; and the viral genome. Release of an intact viral nucleic acid into the environment following capsid destruction is of potential concern since some nucleic acids are infective when liberated from the capsid an aspect that must be considered in viral disinfection. Important considerations in viral inactivation are dealt with by Klein and Deforest (and Prince et al. while an earlier paper by Grossgebauer is highly recommended.

Alcohols: Although several alcohols have been shown to be effective antimicrobials, ethyl alcohol (ethanol, alcohol), isopropyl alcohol (isopropanol, propan-2-ol) and n -propanol (in particular in Europe) are the most widely used (Alcohols exhibit rapid broad-spectrum antimicrobial activity against vegetative bacteria (including mycobacteria), viruses, and fungi but are not sporicidal. They are, however, known to inhibit sporulation and spore germination but this effect is reversible Because of the lack of sporicidal activity, alcohols are not recommended for sterilization but are widely used for both hard-surface disinfection and skin antisepsis. Lower concentrations may also be used as preservatives and to potentiate the activity of other biocides. Many alcohol products include low levels of other biocides (in particular chlorhexidine), which remain on the skin following evaporation of the alcohol, or excipients (including emollients), which decrease the evaporation time of the alcohol and can significantly increase product efficacy In general, isopropyl alcohol is considered slightly more efficacious against bacteria and ethyl alcohol is more potent against viruses however, this is dependent on the concentrations of both the active agent and the test microorganism. For example, isopropyl alcohol has greater lipophilic properties than ethyl alcohol and is less active against hydrophilic viruses (e.g., poliovirus) (Generally, the antimicrobial activity of alcohols is significantly lower at concentrations below 50% and is optimal in the 60 to 90% range.

Little is known about the specific mode of action of alcohols, but based on the increased efficacy in the presence of water, it is generally believed that they cause membrane damage and rapid denaturation of proteins, with subsequent interference with metabolism and cell lysis (This is supported by specific reports of denaturation of Escherichia coli dehydrogenases and an increased lag phase in Enterobacter aerogenes, speculated to be due to inhibition of metabolism required for rapid cell division.

Glutaraldehyde: Glutaraldehyde is an important dialdehyde that has found usage as a disinfectant and sterilant, in particular for low-temperature disinfection and sterilization of endoscopes and surgical equipment and as a fixative in electron icroscopy. Glutaraldehyde has a broad spectrum of activity against bacteria and their spores, fungi, and viruses, and a considerable amount of information is now available about the ways whereby these different organisms are inactivated.

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