Chemical Disinfectants

Guideline for Disinfection and Sterilization in Healthcare Facilities (2008)

AT A GLANCE

Chemical disinfectants from the Guideline for Disinfection and Sterilization in Healthcare Facilities (2008).

ON THIS PAGE

Alcohol

Overview

In the healthcare setting, "alcohol" refers to two water-soluble chemical compounds—ethyl alcohol and isopropyl alcohol—that have generally underrated germicidal characteristics [482]. FDA has not cleared any liquid chemical sterilant or high-level disinfectant with alcohol as the main active ingredient. These alcohols are rapidly bactericidal rather than bacteriostatic against vegetative forms of bacteria; they also are tuberculocidal, fungicidal, and virucidal but do not destroy bacterial spores. Their cidal activity drops sharply when diluted below 50% concentration, and the optimum bactericidal concentration is 60%–90% solutions in water (volume/volume) [483, 484].

Mode of Action

The most feasible explanation for the antimicrobial action of alcohol is denaturation of proteins. This mechanism is supported by the observation that absolute ethyl alcohol, a dehydrating agent, is less bactericidal than mixtures of alcohol and water because proteins are denatured more quickly in the presence of water [484, 485]. Protein denaturation also is consistent with observations that alcohol destroys the dehydrogenases of *Escherichia coli* [486], and that ethyl alcohol increases the lag phase of *Enterobacter aerogenes* [487] and that the lag phase effect could be reversed by adding certain amino acids. The bacteriostatic action was believed caused by inhibition of the production of metabolites essential for rapid cell division.

Microbicidal Activity

Methyl alcohol (methanol) has the weakest bactericidal action of the alcohols and thus seldom is used in healthcare [488]. The bactericidal activity of various concentrations of ethyl alcohol (ethanol) was examined against a variety of microorganisms in exposure periods ranging from 10 seconds to 1 hour [483]. *Pseudomonas aeruginosa* was killed in 10 seconds by all concentrations of ethanol from 30% to 100% (v/v), and *Serratia*

marcescens, E, coli and *Salmonella typhosa* were killed in 10 seconds by all concentrations of ethanol from 40% to 100%. The gram-positive organisms *Staphylococcus aureus* and *Streptococcus pyogenes* were slightly more resistant, being killed in 10 seconds by ethyl alcohol concentrations of 60%–95%. Isopropyl alcohol (isopropanol) was slightly more bactericidal than ethyl alcohol for *E. coli* and *S. aureus* [489].

Ethyl alcohol, 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) [58] or poliovirus) [49]. Isopropyl alcohol is not active against the nonlipid enteroviruses but is fully active against the lipid viruses [72]. Studies also have demonstrated the ability of ethyl and isopropyl alcohol to inactivate the hepatitis B virus(HBV) [224, 225] and the herpes virus, [490] and ethyl alcohol to inactivate human immunodeficiency virus (HIV) [227], rotavirus, echovirus, and astrovirus [491].

In tests of the effect of ethyl alcohol against *M. tuberculosis*, 95% ethanol killed the tubercle bacilli in sputum or water suspension within 15 seconds [492]. In 1964, Spaulding stated that alcohols were the germicide of choice for tuberculocidal activity, and they should be the standard by which all other tuberculocides are compared. For example, he compared the tuberculocidal activity of iodophor (450 ppm), a substituted phenol (3%), and isopropanol (70%/volume) using the mucin-loop test (10^6 *M. tuberculosis* per loop) and determined the contact times needed for complete destruction were 120–180 minutes, 45–60 minutes, and 5 minutes, respectively. The mucin-loop test is a severe test developed to produce long survival times. Thus, these figures should not be extrapolated to the exposure times needed when these germicides are used on medical or surgical material [482].

Ethyl alcohol (70%) was the most effective concentration for killing the tissue phase of *Cryptococcus neoformans*, *Blastomyces dermatitidis*, *Coccidioides immitis*, and *Histoplasma capsulatum* and the culture phases of the latter three organisms aerosolized onto various surfaces. The culture phase was more resistant to the action of ethyl alcohol and required about 20 minutes to disinfect the contaminated surface, compared with <1 minute for the tissue phase [493, 494].

Isopropyl alcohol (20%) is effective in killing the cysts of *Acanthamoeba culbertsoni* (*560*) as are chlorhexidine, hydrogen peroxide, and thimerosal [496].

Uses

Alcohols are not recommended for sterilizing medical and surgical materials principally because they lack sporicidal action and they cannot penetrate protein-rich materials. Fatal postoperative wound infections with *Clostridium* have occurred when alcohols were used to sterilize surgical instruments contaminated with bacterial spores [497]. Alcohols have been used effectively to disinfect oral and rectal thermometers[498, 499], hospital pagers [500], scissors [501], and stethoscopes [502]. Alcohols have been used to disinfect fiberoptic endoscopes [503, 504] but failure of this disinfectant have lead to infection [280, 505]. Alcohol towelettes have been used for years to disinfect small surfaces such as rubber stoppers of multiple-dose medication vials or vaccine bottles. Furthermore, alcohol occasionally is used to disinfect external surfaces of equipment (e.g., stethoscopes, ventilators, manual ventilation bags) [506], CPR manikins [507], ultrasound instruments [508] or medication preparation areas. Two studies demonstrated the effectiveness of 70% isopropyl alcohol to disinfect reusable transducer heads in a controlled environment [509, 510]. In contrast, three bloodstream infection outbreaks have been described when alcohol was used to disinfect transducer heads in an intensive-care setting [511].

The documented shortcomings of alcohols on equipment are that they damage the shellac mountings of lensed instruments, tend to swell and harden rubber and certain plastic tubing after prolonged and repeated use, bleach rubber and plastic tiles [482] and damage tonometer tips (by deterioration of the glue) after the equivalent of 1 working year of routine use [512]. Tonometer biprisms soaked in alcohol for 4 days developed rough front surfaces that potentially could cause corneal damage; this appeared to be caused by weakening of the cementing substances used to fabricate the biprisms [513]. Corneal opacification has been reported when tonometer tips were swabbed with alcohol immediately before measurement of intraocular pressure [514]. Alcohols are flammable and consequently must be stored in a cool, well-ventilated area. They also evaporate rapidly, making extended exposure time difficult to achieve unless the items are immersed.

Chlorine and Chlorine Compounds

Overview

Hypochlorites, the most widely used of the chlorine disinfectants, are available as liquid (e.g., sodium hypochlorite) or solid (e.g., calcium hypochlorite). The most prevalent chlorine products in the United States are aqueous solutions of 5.25%–6.15% sodium hypochlorite (see glossary), usually called household bleach. They have a broad spectrum of antimicrobial activity, do not leave toxic residues, are unaffected by water hardness, are inexpensive and fast acting [328], remove dried or fixed organisms and biofilms from surfaces[465], and have a low incidence of serious toxicity [515-517]. Sodium hypochlorite at the concentration used in household bleach (5.25-6.15%) can produce ocular irritation or oropharyngeal, esophageal, and gastric burns [318, 518-522]. Other disadvantages of hypochlorites include corrosiveness to metals in high concentrations (>500 ppm), inactivation by organic matter, discoloring or "bleaching" of fabrics, release of toxic chlorine gas when mixed with

ammonia or acid (e.g., household cleaning agents) [523-525], and relative stability [327]. The microbicidal activity of chlorine is attributed largely to undissociated hypochlorous acid (HOCl). The dissociation of HOCl to the less microbicidal form (hypochlorite ion OCl^-) depends on pH. The disinfecting efficacy of chlorine decreases with an increase in pH that parallels the conversion of undissociated HOCl to OCl^- [329, 526]. A potential hazard is production of the carcinogen bis(chloromethyl) ether when hypochlorite solutions contact formaldehyde [527] and the production of the animal carcinogen trihalomethane when hot water is hyperchlorinated [528]. After reviewing environmental fate and ecologic data, EPA has determined the currently registered uses of hypochlorites will not result in unreasonable adverse effects to the environment [529].

Alternative compounds that release chlorine and are used in the health-care setting include demand-release chlorine dioxide, sodium dichloroisocyanurate, and chloramine-T. The advantage of these compounds over the hypochlorites is that they retain chlorine longer and so exert a more prolonged bactericidal effect. Sodium dichloroisocyanurate tablets are stable, and for two reasons, the microbicidal activity of solutions prepared from sodium dichloroisocyanurate tablets might be greater than that of sodium hypochlorite solutions containing the same total available chlorine. First, with sodium dichloroisocyanurate, only 50% of the total available chlorine is free (HOCl and OCl^-), whereas the remainder is combined (monochloroisocyanurate or dichloroisocyanurate), and as free available chlorine is used up, the latter is released to restore the equilibrium. Second, solutions of sodium dichloroisocyanurate are acidic, whereas sodium hypochlorite solutions are alkaline, and the more microbicidal type of chlorine (HOCl) is believed to predominate [530-533]. Chlorine dioxide-based disinfectants are prepared fresh as required by mixing the two components (base solution [citric acid with preservatives and corrosion inhibitors] and the activator solution [sodium chlorite]). In vitro suspension tests showed that solutions containing about 140 ppm chlorine dioxide achieved a reduction factor exceeding 10^6 of *S. aureus* in 1 minute and of *Bacillus atrophaeus* spores in 2.5 minutes in the presence of 3 g/L bovine albumin. The potential for damaging equipment requires consideration because long-term use can damage the outer plastic coat of the insertion tube [534]. In another study, chlorine dioxide solutions at either 600 ppm or 30 ppm killed *Mycobacterium avium-intracellulare* within 60 seconds after contact but contamination by organic material significantly affected the microbicidal properties[535].

The microbicidal activity of a new disinfectant, "superoxidized water," has been examined The concept of electrolyzing saline to create a disinfectant or antiseptics is appealing because the basic materials of saline and electricity are inexpensive and the end product (i.e., water) does not damage the environment. The main products of this water are hypochlorous acid (e.g., at a concentration of about 144 mg/L) and chlorine. As with any germicide, the antimicrobial activity of superoxidized water is strongly affected by the concentration of the active ingredient (available free chlorine) [536]. One manufacturer generates the disinfectant at the point of use by passing a saline solution over coated titanium electrodes at 9 amps. The product generated has a pH of 5.0–6.5 and an oxidation-reduction potential (redox) of >950 mV. Although superoxidized water is intended to be generated fresh at the point of use, when tested under clean conditions the disinfectant was effective within 5 minutes when 48 hours old [537]. Unfortunately, the equipment required to produce the product can be expensive because parameters such as pH, current, and redox potential must be closely monitored. The solution is nontoxic to biologic tissues. Although the United Kingdom manufacturer claims the solution is noncorrosive and nondamaging to endoscopes and processing equipment, one flexible endoscope manufacturer (Olympus Key-Med, United Kingdom) has voided the warranty on the endoscopes if superoxidized water is used to disinfect them [538]. As with any germicide formulation, the user should check with the device manufacturer for compatibility with the germicide. Additional studies are needed to determine whether this solution could be used as an alternative to other disinfectants or antiseptics for hand washing, skin antisepsis, room cleaning, or equipment disinfection (e.g., endoscopes, dialyzers) [400, 539, 540]. In October 2002, the FDA cleared superoxidized water as a high-level disinfectant (FDA, personal communication, September 18, 2002).

Mode of Action

The exact mechanism by which free chlorine destroys microorganisms has not been elucidated. Inactivation by chlorine can result from a number of factors: oxidation of sulfhydryl enzymes and amino acids; ring chlorination of amino acids; loss of intracellular contents; decreased uptake of nutrients; inhibition of protein synthesis; decreased oxygen uptake; oxidation of respiratory components; decreased adenosine triphosphate production; breaks in DNA; and depressed DNA synthesis [329, 347]. The actual microbicidal mechanism of chlorine might involve a combination of these factors or the effect of chlorine on critical sites [347].

Microbicidal Activity

Low concentrations of free available chlorine (e.g., HOCl, OCl^-, and elemental chlorine-Cl_2) have a biocidal effect on mycoplasma (25 ppm) and vegetative bacteria (<5 ppm) in seconds in the absence of an organic load [329, 418]. Higher concentrations (1,000 ppm) of chlorine are required to kill *M. tuberculosis* using the Association of Official Analytical Chemists (AOAC) tuberculocidal test [73]. A concentration of 100 ppm will kill ≥99.9% of *B. atrophaeus* spores within 5 minutes [541, 542] and destroy mycotic agents in <1 hour [329]. Acidified bleach and regular bleach (5,000 ppm chlorine) can inactivate 10^6 *Clostridium difficile* spores in ≤10 minutes [262]. One study reported that 25 different viruses were inactivated in 10 minutes with 200 ppm available chlorine [72]. Several studies have demonstrated the effectiveness of diluted sodium hypochlorite and other disinfectants to inactivate HIV [61]. Chlorine (500 ppm) showed inhibition of *Candida* after 30 seconds of exposure [54]. In experiments using the AOAC Use-Dilution Method, 100 ppm of free chlorine killed 10^6–10^7 *S. aureus*, *Salmonella choleraesuis*, and *P. aeruginosa* in <10 minutes [327]. Because household bleach contains 5.25%–6.15% sodium hypochlorite, or 52,500–61,500 ppm available chlorine, a 1:1,000 dilution provides about 53–62 ppm available chlorine, and a 1:10 dilution of household bleach provides about 5250–6150 ppm.

Data are available for chlorine dioxide that support manufacturers' bactericidal, fungicidal, sporicidal, tuberculocidal, and virucidal label claims [543-546]. A chlorine dioxide generator has been shown effective for decontaminating flexible endoscopes [534] but it is not currently FDA-cleared for use as a high-level disinfectant [85]. Chlorine dioxide can be produced by mixing solutions, such as a solution of chlorine with a solution of sodium chlorite [329]. In 1986, a chlorine dioxide product was voluntarily removed from the market when its use caused leakage of cellulose-based dialyzer membranes, which allowed bacteria to migrate from the dialysis fluid side of the dialyzer to the blood side [547].

Sodium dichloroisocyanurate at 2,500 ppm available chlorine is effective against bacteria in the presence of up to 20% plasma, compared with 10% plasma for sodium hypochlorite at 2,500 ppm [548].

"Superoxidized water" has been tested against bacteria, mycobacteria, viruses, fungi, and spores [537, 539, 549]. Freshly generated superoxidized water is rapidly effective (<2 minutes) in achieving a 5-$\log_{10}$ reduction of pathogenic microorganisms (i.e., *M. tuberculosis*, *M. chelonae*, poliovirus, HIV, multidrug-resistant *S. aureus*, *E. coli, Candida albicans*, *Enterococcus faecalis, P. aeruginosa*) in the absence of organic loading. However, the biocidal activity of this disinfectant decreased substantially in the presence of organic material (e.g., 5% horse serum) [537, 549, 550]. No bacteria or viruses were detected on artificially contaminated endoscopes after a 5-minute exposure to superoxidized water [551] and HBV-DNA was not detected from any endoscope experimentally contaminated with HBV-positive mixed sera after a disinfectant exposure time of 7 minutes[552].

Uses

Hypochlorites are widely used in healthcare facilities in a variety of settings. [328] Inorganic chlorine solution is used for disinfecting tonometer heads [188] and for spot-disinfection of countertops and floors. A 1:10–1:100 dilution of 5.25%–6.15% sodium hypochlorite (i.e., household bleach) [22, 228, 553, 554] or an EPA-registered tuberculocidal disinfectant [17]has been recommended for decontaminating blood spills. For small spills of blood (i.e., drops of blood) on noncritical surfaces, the area can be disinfected with a 1:100 dilution of 5.25%-6.15% sodium hypochlorite or an EPA-registered tuberculocidal disinfectant. Because hypochlorites and other germicides are substantially inactivated in the presence of blood [63, 548, 555, 556], large spills of blood require that the surface be cleaned before an EPA-registered disinfectant or a 1:10 (final concentration) solution of household bleach is applied [557]. If a sharps injury is possible, the surface initially should be decontaminated [69, 318], then cleaned and disinfected (1:10 final concentration) [63]. Extreme care always should be taken to prevent percutaneous injury. At least 500 ppm available chlorine for 10 minutes is recommended for decontaminating CPR training manikins [558]. Full-strength bleach has been recommended for self-disinfection of needles and syringes used for illicit-drug injection when needle-exchange programs are not available. The difference in the recommended concentrations of bleach reflects the difficulty of cleaning the interior of needles and syringes and the use of needles and syringes for parenteral injection [559]. Clinicians should not alter their use of chlorine on environmental surfaces on the basis of testing methodologies that do not simulate actual disinfection practices [560, 561]. Other uses in healthcare include as an irrigating agent in endodontic treatment [562] and as a disinfectant for manikins, laundry, dental appliances, hydrotherapy tanks [23, 41], regulated medical waste before disposal [328], and the water distribution system in hemodialysis centers and hemodialysis machines [563].

Chlorine long has been used as the disinfectant in water treatment. Hyperchlorination of a *Legionella*-contaminated hospital water system [23] resulted in a dramatic decrease (from 30% to 1.5%) in the isolation of *L. pneumophila* from water outlets and a cessation of healthcare-associated Legionnaires' disease in an affected unit [528, 564]. Water disinfection with monochloramine by municipal water-treatment plants substantially reduced the risk for healthcare–associated Legionnaires disease [565, 566]. Chlorine dioxide also has been used to control *Legionella* in a hospital water supply. [567] Chloramine T [568] and hypochlorites [41] have been used to disinfect hydrotherapy equipment.

Hypochlorite solutions in tap water at a pH >8 stored at room temperature (23°C) in closed, opaque plastic containers can lose up to 40%–50% of their free available chlorine level over 1 month. Thus, if a user wished to have a solution containing 500 ppm of available chlorine at day 30, he or she should prepare a solution containing 1,000 ppm of chlorine at time 0. Sodium hypochlorite solution does not decompose after 30 days when stored in a closed brown bottle [327].

The use of powders, composed of a mixture of a chlorine-releasing agent with highly absorbent resin, for disinfecting spills of body fluids has been evaluated by laboratory tests and hospital ward trials. The inclusion of acrylic resin particles in formulations markedly increases the volume of fluid that can be soaked up because the resin can absorb 200–300 times its own weight of fluid, depending on the fluid consistency. When experimental formulations containing 1%, 5%, and 10% available chlorine were evaluated by a standardized surface test, those containing 10% demonstrated bactericidal activity. One problem with chlorine-releasing granules is that they can generate chlorine fumes when applied to urine [569].

Formaldehyde

Overview

Formaldehyde is used as a disinfectant and sterilant in both its liquid and gaseous states. Liquid formaldehyde will be considered briefly in this section, and the gaseous form is reviewed elsewhere [570]. Formaldehyde is sold and used principally as a water-based solution called formalin, which is 37% formaldehyde by weight. The aqueous solution is a bactericide, tuberculocide, fungicide, virucide and sporicide [72, 82, 571-573]. OSHA indicated that formaldehyde should be handled in the workplace as a potential carcinogen and set an employee exposure standard for formaldehyde that limits an 8-hour time-weighted average exposure concentration of 0.75 ppm [574, 575]. The standard includes a second permissible exposure limit in the form of a short-term exposure limit (STEL) of 2 ppm that is the maximum exposure allowed during a 15-minute period [576]. Ingestion of formaldehyde can be fatal, and long-term exposure to low levels in the air or on the skin can cause asthma-like respiratory problems and skin irritation, such as dermatitis and itching. For these reasons, employees should have limited direct contact with formaldehyde, and these considerations limit its role in sterilization and disinfection processes. Key provisions of the OSHA standard that protects workers from exposure to formaldehyde appear in Title 29 of the Code of Federal Regulations (CFR) Part 1910.1048 (and equivalent regulations in states with OSHA-approved state plans) [577].

Mode of Action

Formaldehyde inactivates microorganisms by alkylating the amino and sulfhydral groups of proteins and ring nitrogen atoms of purine bases [376].

Microbicidal Activity

Varying concentrations of aqueous formaldehyde solutions destroy a wide range of microorganisms. Inactivation of poliovirus in 10 minutes required an 8% concentration of formalin, but all other viruses tested were inactivated with 2% formalin [72]. Four percent formaldehyde is a tuberculocidal agent, inactivating 10^4 *M. tuberculosis* in 2 minutes [82], and 2.5% formaldehyde inactivated about 10^7 *Salmonella* Typhi in 10 minutes in the presence of organic matter [572]. The sporicidal action of formaldehyde was slower than that of glutaraldehyde in comparative tests with 4% aqueous formaldehyde and 2% glutaraldehyde against the spores of *B. anthracis* [82]. The formaldehyde solution required 2 hours of contact to achieve an inactivation factor of 10^4, whereas glutaraldehyde required only 15 minutes.

Uses

Although formaldehyde-alcohol is a chemical sterilant and formaldehyde is a high-level disinfectant, the health-care uses of formaldehyde are limited by its irritating fumes and its pungent odor even at very low levels (<1 ppm). For these reasons and others—such as its role as a suspected human carcinogen linked to nasal cancer and lung cancer [578], this germicide is excluded from Table 1. When it is used, , direct exposure to employees generally is limited; however, excessive exposures to formaldehyde have been documented for employees of renal transplant units [574, 579], and students in a gross anatomy laboratory [580]. Formaldehyde is used in the health-care setting to prepare viral vaccines (e.g., poliovirus and influenza); as an embalming agent; and to preserve anatomic specimens; and historically has been used to sterilize surgical instruments, especially when mixed with ethanol. A 1997 survey found that formaldehyde was used for reprocessing hemodialyzers by 34% of U.S. hemodialysis centers—a 60% decrease from 1983 [249, 581]. If used at room temperature, a concentration of 4% with a minimum exposure of 24 hours is required to disinfect disposable hemodialyzers reused on the same patient [582, 583]. Aqueous formaldehyde solutions (1%–2%) also have been used to disinfect the internal fluid pathways of dialysis machines [583]. To minimize a potential health hazard to dialysis patients, the dialysis equipment must be thoroughly rinsed and tested for residual formaldehyde before use.

Paraformaldehyde, a solid polymer of formaldehyde, can be vaporized by heat for the gaseous decontamination of laminar flow biologic safety cabinets when maintenance work or filter changes require access to the sealed portion of the cabinet.

Glutaraldehyde

Overview

Glutaraldehyde is a saturated dialdehyde that has gained wide acceptance as a high-level disinfectant and chemical sterilant [107]. Aqueous solutions of glutaraldehyde are acidic and generally in this state are not sporicidal. Only when the solution is "activated" (made alkaline) by use of alkalinating agents to pH 7.5–8.5 does the solution become sporicidal. Once activated, these solutions have a shelf-life of minimally 14 days because of the polymerization of the glutaraldehyde molecules at alkaline pH levels. This polymerization blocks the active sites (aldehyde groups) of the glutaraldehyde molecules that are responsible for its biocidal activity.

Novel glutaraldehyde formulations (e.g., glutaraldehyde-phenol-sodium phenate, potentiated acid glutaraldehyde, stabilized alkaline glutaraldehyde) produced in the past 30 years have overcome the problem of rapid loss of activity (e.g., use-life 28–30 days) while generally maintaining excellent microbicidal activity [584-588]. However, antimicrobial activity depends not only on age but also on use conditions, such as dilution and organic stress. Manufacturers' literature for these preparations suggests the neutral or alkaline glutaraldehydes possess microbicidal and anticorrosion properties superior to those of acid glutaraldehydes, and a few published reports substantiate these claims [542, 589, 590]. However, two studies found no difference in the microbicidal activity of alkaline and acid glutaraldehydes [73, 591]. The use of

glutaraldehyde-based solutions in health-care facilities is widespread because of their advantages, including excellent biocidal properties; activity in the presence of organic matter (20% bovine serum); and noncorrosive action to endoscopic equipment, thermometers, rubber, or plastic equipment (Tables 4 and 5).

Mode of Action

The biocidal activity of glutaraldehyde results from its alkylation of sulfhydryl, hydroxyl, carboxyl, and amino groups of microorganisms, which alters RNA, DNA, and protein synthesis. The mechanism of action of glutaraldehydes are reviewed extensively elsewhere [592, 593].

Microbicidal Activity

The in vitro inactivation of microorganisms by glutaraldehydes has been extensively investigated and reviewed [592, 593]. Several investigators showed that ≥2% aqueous solutions of glutaraldehyde, buffered to pH 7.5–8.5 with sodium bicarbonate effectively killed vegetative bacteria in <2 minutes; *M. tuberculosis*, fungi, and viruses in <10 minutes; and spores of *Bacillus* and *Clostridium* species in 3 hours [542, 592-597]. Spores of *C. difficile* are more rapidly killed by 2% glutaraldehyde than are spores of other species of *Clostridium* and *Bacillus* [79, 265, 266]. Microorganisms with substantial resistance to glutaraldehyde have been reported, including some mycobacteria (*M. chelonae*, *Mycobacterium avium-intracellulare, M. xenopi*) [598-601], *Methylobacterium mesophilicum* [602], *Trichosporon*, fungal ascospores (e.g., *Microascus cinereus*, *Cheatomium globosum*), and *Cryptosporidium*[271, 603]. *M. chelonae* persisted in a 0.2% glutaraldehyde solution used to store porcine prosthetic heart valves [604].

Two percent alkaline glutaraldehyde solution inactivated 10^5 *M. tuberculosis* cells on the surface of penicylinders within 5 minutes at 18°C [589]. However, subsequent studies[82] questioned the mycobactericidal prowess of glutaraldehydes. Two percent alkaline glutaraldehyde has slow action (20 to >30 minutes) against *M. tuberculosis* and compares unfavorably with alcohols, formaldehydes, iodine, and phenol [82]. Suspensions of *M. avium, M. intracellulare,* and *M. gordonae* were more resistant to inactivation by a 2% alkaline glutaraldehyde (estimated time to complete inactivation: ~60 minutes) than were virulent *M. tuberculosis* (estimated time to complete inactivation ~25 minutes) [605]. The rate of kill was directly proportional to the temperature, and a standardized suspension of *M. tuberculosis* could not be sterilized within 10 minutes [84]. An FDA-cleared chemical sterilant containing 2.5% glutaraldehyde uses increased temperature (35°C) to reduce the time required to achieve high-level disinfection (5 minutes) [85, 606], but its use is limited to automatic endoscope reprocessors equipped with a heater. In another study employing membrane filters for measurement of mycobactericidal activity of 2% alkaline glutaraldehyde, complete inactivation was achieved within 20 minutes at 20°C when the test inoculum was 10^6 *M. tuberculosis* per membrane [81]. Several investigators [55, 57, 73, 76, 80, 81, 84, 605] have demonstrated that glutaraldehyde solutions inactivate 2.4 to >5.0 $\log_{10}$ of *M. tuberculosis* in 10 minutes (including multidrug-resistant *M. tuberculosis*) and 4.0–6.4 $\log_{10}$ of *M. tuberculosis* in 20 minutes. On the basis of these data and other studies, 20 minutes at room temperature is considered the minimum exposure time needed to reliably kill *Mycobacteria* and other vegetative bacteria with ≥2% glutaraldehyde [17, 19, 27, 57, 83, 94, 108, 111, 117-121, 607].

Glutaraldehyde is commonly diluted during use, and studies showed a glutaraldehyde concentration decline after a few days of use in an automatic endoscope washer [608, 609]. The decline occurs because instruments are not thoroughly dried and water is carried in with the instrument, which increases the solution's volume and dilutes its effective concentration [610]. This emphasizes the need to ensure that semicritical equipment is disinfected with an acceptable concentration of glutaraldehyde. Data suggest that 1.0%–1.5% glutaraldehyde is the minimum effective concentration for >2% glutaraldehyde solutions when used as a high-level disinfectant [76, 589, 590, 609]. Chemical test strips or liquid chemical monitors [610, 611] are available for determining whether an effective concentration of glutaraldehyde is present despite repeated use and dilution. The frequency of testing should be based on how frequently the solutions are used (e.g., used daily, test daily; used weekly, test before use; used 30 times per day, test each 10th use), but the strips should not be used to extend the use life beyond the expiration date. Data suggest the chemicals in the test strip deteriorate with time [612] and a manufacturer's expiration date should be placed on the bottles. The bottle of test strips should be dated when opened and used for the period of time indicated on the bottle (e.g., 120 days). The results of test strip monitoring should be documented. The glutaraldehyde test kits have been preliminarily evaluated for accuracy and range [612] but the reliability has been questioned [613]. To ensure the presence of minimum effective concentration of the high-level disinfectant, manufacturers of some chemical test strips recommend the use of quality-control procedures to ensure the strips perform properly. If the manufacturer of the chemical test strip recommends a quality-control procedure, users should comply with the manufacturer's recommendations. The concentration should be considered unacceptable or unsafe when the test indicates a dilution below the product's minimum effective concentration (MEC) (generally to ≤1.0%–1.5% glutaraldehyde) by the indicator not changing color.

A 2.0% glutaraldehyde–7.05% phenol–1.20% sodium phenate product that contained 0.125% glutaraldehyde–0.44% phenol–0.075% sodium phenate when diluted 1:16 is not recommended as a high-level disinfectant because it lacks bactericidal activity in the presence of organic matter and lacks tuberculocidal, fungicidal, virucidal, and sporicidal activity [49, 55, 56, 71, 73-79, 614]. In December 1991, EPA issued an order to stop the sale of all batches of this product because of efficacy data showing the product is not effective against spores and possibly other microorganisms or inanimate objects as claimed on the label [615]. FDA has cleared a glutaraldehyde–phenol/phenate concentrate as a high-level

disinfectant that contains 1.12% glutaraldehyde with 1.93% phenol/phenate at its use concentration. Other FDA cleared glutaraldehyde sterilants that contain 2.4%–3.4% glutaraldehyde are used undiluted [606].

Uses

Glutaraldehyde is used most commonly as a high-level disinfectant for medical equipment such as endoscopes [69, 107, 504], spirometry tubing, dialyzers [616], transducers, anesthesia and respiratory therapy equipment [617], hemodialysis proportioning and dialysate delivery systems [249, 618], and reuse of laparoscopic disposable plastic trocars [619]. Glutaraldehyde is noncorrosive to metal and does not damage lensed instruments, rubber. or plastics. Glutaraldehyde should not be used for cleaning noncritical surfaces because it is too toxic and expensive.

Colitis believed caused by glutaraldehyde exposure from residual disinfecting solution in endoscope solution channels has been reported and is preventable by careful endoscope rinsing [318, 620-630]. One study found that residual glutaraldehyde levels were higher and more variable after manual disinfection (<0.2 mg/L to 159.5 mg/L) than after automatic disinfection (0.2–6.3 mg/L)[631]. Similarly, keratopathy and corneal decompensation were caused by ophthalmic instruments that were inadequately rinsed after soaking in 2% glutaraldehyde [632, 633].

Healthcare personnel can be exposed to elevated levels of glutaraldehyde vapor when equipment is processed in poorly ventilated rooms, when spills occur, when glutaraldehyde solutions are activated or changed,[634], or when open immersion baths are used. Acute or chronic exposure can result in skin irritation or dermatitis, mucous membrane irritation (eye, nose, mouth), or pulmonary symptoms [318, 635-639]. Epistaxis, allergic contact dermatitis, asthma, and rhinitis also have been reported in healthcare workers exposed to glutaraldehyde [636, 640-647].

Glutaraldehyde exposure should be monitored to ensure a safe work environment. Testing can be done by four techniques: a silica gel tube/gas chromatography with a flame ionization detector, dinitrophenylhydrazine (DNPH)-impregnated filter cassette/high-performance liquid chromatography (HPLC) with an ultraviolet (UV) detector, a passive badge/HPLC, or a handheld glutaraldehyde air monitor [648]. The silica gel tube and the DNPH-impregnated cassette are suitable for monitoring the 0.05 ppm ceiling limit. The passive badge, with a 0.02 ppm limit of detection, is considered marginal at the Americal Council of Governmental Industrial Hygienists (ACGIH) ceiling level. The ceiling level is considered too close to the glutaraldehyde meter's 0.03 ppm limit of detection to provide confidence in the readings [648]. ACGIH does not require a specific monitoring schedule for glutaraldehyde; however, a monitoring schedule is needed to ensure the level is less than the ceiling limit. For example, monitoring should be done initially to determine glutaraldehyde levels, after procedural or equipment changes, and in response to worker complaints [649]. In the absence of an OSHA permissible exposure limit, if the glutaraldehyde level is higher than the ACGIH ceiling limit of 0.05 ppm, corrective action and repeat monitoring would be prudent [649].

Engineering and work-practice controls that can be used to resolve these problems include ducted exhaust hoods, air systems that provide 7–15 air exchanges per hour, ductless fume hoods with absorbents for the glutaraldehyde vapor, tight-fitting lids on immersion baths, personal protection (e.g., nitrile or butyl rubber gloves but not natural latex gloves, goggles) to minimize skin or mucous membrane contact, and automated endoscope processors [7, 650]. If engineering controls fail to maintain levels below the ceiling limit, institutions can consider the use of respirators (e.g., a half-face respirator with organic vapor cartridge [640] or a type "C" supplied air respirator with a full facepiece operated in a positive pressure mode) [651]. In general, engineering controls are preferred over work-practice and administrative controls because they do not require active participation by the health-care worker. Even though enforcement of the OSHA ceiling limit was suspended in 1993 by the U.S. Court of Appeals [577], limiting employee exposure to 0.05 ppm (according to ACGIH) is prudent because, at this level, glutaraldehyde can irritate the eyes, throat, and nose [318, 577, 639, 652]. If glutaraldehyde disposal through the sanitary sewer system is restricted, sodium bisulfate can be used to neutralize the glutaraldehyde and make it safe for disposal.

Hydrogen Peroxide

Overview

The literature contains several accounts of the properties, germicidal effectiveness, and potential uses for stabilized hydrogen peroxide in the health-care setting. Published reports ascribe good germicidal activity to hydrogen peroxide and attest to its bactericidal, virucidal, sporicidal, and fungicidal properties [653-655]. (Tables 4 and 5) The FDA website lists cleared liquid chemical sterilants and high-level disinfectants containing hydrogen peroxide and their cleared contact conditions.

Mode of Action

Hydrogen peroxide works by producing destructive hydroxyl free radicals that can attack membrane lipids, DNA, and other essential cell components. Catalase, produced by aerobic organisms and facultative anaerobes that possess cytochrome systems, can protect cells from metabolically produced hydrogen peroxide by degrading hydrogen peroxide to water and oxygen. This defense is overwhelmed by the concentrations used for disinfection [653, 654].

Microbicidal Activity

Hydrogen peroxide is active against a wide range of microorganisms, including bacteria, yeasts, fungi, viruses, and spores [78, 654]. A 0.5% accelerated hydrogen peroxide demonstrated bactericidal and virucidal activity in 1 minute and mycobactericidal and fungicidal activity in 5 minutes [656]. Bactericidal effectiveness and stability of hydrogen peroxide in urine has been demonstrated against a variety of health-care–associated pathogens; organisms with high cellular catalase activity (e.g., *S. aureus*, *S. marcescens*, and *Proteus mirabilis*) required 30–60 minutes of exposure to 0.6% hydrogen peroxide for a 10^8 reduction in cell counts, whereas organisms with lower catalase activity (e.g., *E. coli*, S*treptococcus* species, and *Pseudomonas* species) required only 15 minutes' exposure [657]. In an investigation of 3%, 10%, and 15% hydrogen peroxide for reducing spacecraft bacterial populations, a complete kill of 10^6 spores (i.e., *Bacillus* species) occurred with a 10% concentration and a 60-minute exposure time. A 3% concentration for 150 minutes killed 10^6 spores in six of seven exposure trials [658]. A 10% hydrogen peroxide solution resulted in a 10^3 decrease in *B. atrophaeus* spores, and a $\geq 10^5$ decrease when tested against 13 other pathogens in 30 minutes at 20°C [659, 660]. A 3.0% hydrogen peroxide solution was ineffective against VRE after 3 and 10 minutes exposure times [661] and caused only a 2-$\log_{10}$ reduction in the number of *Acanthamoeba* cysts in approximately 2 hours [662]. A 7% stabilized hydrogen peroxide proved to be sporicidal (6 hours of exposure), mycobactericidal (20 minutes), fungicidal (5 minutes) at full strength, virucidal (5 minutes) and bactericidal (3 minutes) at a 1:16 dilution when a quantitative carrier test was used [655]. The 7% solution of hydrogen peroxide, tested after 14 days of stress (in the form of germ-loaded carriers and respiratory therapy equipment), was sporicidal (>7 $\log_{10}$ reduction in 6 hours), mycobactericidal (>6.5 $\log_{10}$ reduction in 25 minutes), fungicidal (>5 $\log_{10}$ reduction in 20 minutes), bactericidal (>6 $\log_{10}$ reduction in 5 minutes) and virucidal (5 $\log_{10}$ reduction in 5 minutes) [663]. Synergistic sporicidal effects were observed when spores were exposed to a combination of hydrogen peroxide (5.9%–23.6%) and peracetic acid [664]. Other studies demonstrated the antiviral activity of hydrogen peroxide against rhinovirus [665]. The time required for inactivating three serotypes of rhinovirus using a 3% hydrogen peroxide solution was 6–8 minutes; this time increased with decreasing concentrations (18-20 minutes at 1.5%, 50–60 minutes at 0.75%).

Concentrations of hydrogen peroxide from 6% to 25% show promise as chemical sterilants. The product marketed as a sterilant is a premixed, ready-to-use chemical that contains 7.5% hydrogen peroxide and 0.85% phosphoric acid (to maintain a low pH) [69]. The mycobactericidal activity of 7.5% hydrogen peroxide has been corroborated in a study showing the inactivation of $>10^5$ multidrug-resistant *M. tuberculosis* after a 10-minute exposure [666]. Thirty minutes were required for >99.9% inactivation of poliovirus and HAV [667]. Three percent and 6% hydrogen peroxide were unable to inactivate HAV in 1 minute in a carrier test [58]. When the effectiveness of 7.5% hydrogen peroxide at 10 minutes was compared with 2% alkaline glutaraldehyde at 20 minutes in manual disinfection of endoscopes, no significant difference in germicidal activity was observed [668].). No complaints were received from the nursing or medical staff regarding odor or toxicity. In one study, 6% hydrogen peroxide (unused product was 7.5%) was more effective in the high-level disinfection of flexible endoscopes than was the 2% glutaraldehyde solution [456]. A new, rapid-acting 13.4% hydrogen peroxide formulation (that is not yet FDA-cleared) has demonstrated sporicidal, mycobactericidal, fungicidal, and virucidal efficacy. Manufacturer data demonstrate that this solution sterilizes in 30 minutes and provides high-level disinfection in 5 minutes[669]. This product has not been used long enough to evaluate material compatibility to endoscopes and other semicritical devices, and further assessment by instrument manufacturers is needed.

Under normal conditions, hydrogen peroxide is extremely stable when properly stored (e.g., in dark containers). The decomposition or loss of potency in small containers is less than 2% per year at ambient temperatures [670].

Uses

Commercially available 3% hydrogen peroxide is a stable and effective disinfectant when used on inanimate surfaces. It has been used in concentrations from 3% to 6% for disinfecting soft contact lenses (e.g., 3% for 2–3 hrs) [653, 671, 672], tonometer biprisms [513], ventilators [673], fabrics [397], and endoscopes [456]. Hydrogen peroxide was effective in spot-disinfecting fabrics in patients' rooms [397]. Corneal damage from a hydrogen peroxide-soaked tonometer tip that was not properly rinsed has been reported [674]. Hydrogen peroxide also has been instilled into urinary drainage bags in an attempt to eliminate the bag as a source of bladder bacteriuria and environmental contamination [675]. Although the instillation of hydrogen peroxide into the bag reduced microbial contamination of the bag, this procedure did not reduce the incidence of catheter-associated bacteriuria [675].

A chemical irritation resembling pseudomembranous colitis caused by either 3% hydrogen peroxide or a 2% glutaraldehyde has been reported [621]. An epidemic of pseudomembrane-like enteritis and colitis in seven patients in a gastrointestinal endoscopy unit also has been associated with inadequate rinsing of 3% hydrogen peroxide from the endoscope [676].

As with other chemical sterilants, dilution of the hydrogen peroxide must be monitored by regularly testing the minimum effective concentration (i.e., 7.5%–6.0%). Compatibility testing by Olympus America of the 7.5% hydrogen peroxide found both cosmetic changes (e.g., discoloration of black anodized metal finishes) [69] and functional changes with the tested endoscopes (Olympus, written communication, October 15, 1999).

Iodophors

Overview

Iodine solutions or tinctures long have been used by health professionals primarily as antiseptics on skin or tissue. Iodophors, on the other hand, have been used both as antiseptics and disinfectants. FDA has not cleared any liquid chemical sterilant or high-level disinfectants with iodophors as the main active ingredient. An iodophor is a combination of iodine and a solubilizing agent or carrier; the resulting complex provides a sustained-release reservoir of iodine and releases small amounts of free iodine in aqueous solution. The best-known and most widely used iodophor is povidone-iodine, a compound of polyvinylpyrrolidone with iodine. This product and other iodophors retain the germicidal efficacy of iodine but unlike iodine generally are nonstaining and relatively free of toxicity and irritancy [677, 678].

Several reports that documented intrinsic microbial contamination of antiseptic formulations of povidone-iodine and poloxamer-iodine [679-681] caused a reappraisal of the chemistry and use of iodophors[682]. "Free" iodine (I_2) contributes to the bactericidal activity of iodophors and dilutions of iodophors demonstrate more rapid bactericidal action than does a full-strength povidone-iodine solution. The reason for the observation that dilution increases bactericidal activity is unclear, but dilution of povidone-iodine might weaken the iodine linkage to the carrier polymer with an accompanying increase of free iodine in solution [680]. Therefore, iodophors must be diluted according to the manufacturers' directions to achieve antimicrobial activity.

Mode of Action

Iodine can penetrate the cell wall of microorganisms quickly, and the lethal effects are believed to result from disruption of protein and nucleic acid structure and synthesis.

Microbicidal Activity

Published reports on the in vitro antimicrobial efficacy of iodophors demonstrate that iodophors are bactericidal, mycobactericidal, and virucidal but can require prolonged contact times to kill certain fungi and bacterial spores [14, 71-73, 290, 683-686]. Three brands of povidone-iodine solution have demonstrated more rapid kill (seconds to minutes) of *S. aureus* and *M. chelonae* at a 1:100 dilution than did the stock solution [683]. The virucidal activity of 75–150 ppm available iodine was demonstrated against seven viruses [72]. Other investigators have questioned the efficacy of iodophors against poliovirus in the presence of organic matter [685]and rotavirus SA-11 in distilled or tapwater [290]. Manufacturers' data demonstrate that commercial iodophors are not sporicidal, but they are tuberculocidal, fungicidal, virucidal, and bactericidal at their recommended use-dilution.

Uses

Besides their use as an antiseptic, iodophors have been used for disinfecting blood culture bottles and medical equipment, such as hydrotherapy tanks, thermometers, and endoscopes. Antiseptic iodophors are not suitable for use as hard-surface disinfectants because of concentration differences. Iodophors formulated as antiseptics contain less free iodine than do those formulated as disinfectants [376]. Iodine or iodine-based antiseptics should not be used on silicone catheters because they can adversely affect the silicone tubing [687].

Ortho-phthalaldehyde (OPA)

Overview

Ortho-phthalaldehyde is a high-level disinfectant that received FDA clearance in October 1999. It contains 0.55% 1,2-benzenedicarboxaldehyde (OPA). OPA solution is a clear, pale-blue liquid with a pH of 7.5. (Tables 4 and 5)

Mode of Action

Preliminary studies on the mode of action of OPA suggest that both OPA and glutaraldehyde interact with amino acids, proteins, and microorganisms. However, OPA is a less potent cross-linking agent. This is compensated for by the lipophilic aromatic nature of OPA that is likely to assist its uptake through the outer layers of mycobacteria and gram-negative bacteria [688-690]. OPA appears to kill spores by blocking the spore germination process [691].

Microbicidal Activity

Studies have demonstrated excellent microbicidal activity in vitro [69, 100, 271, 400, 692-703]. For example, OPA has superior mycobactericidal activity (5-$\log_{10}$ reduction in 5 minutes) to glutaraldehyde. The mean times required to produce a 6-$\log_{10}$ reduction for *M. bovis* using 0.21% OPA was 6 minutes, compared with 32 minutes using 1.5% glutaraldehyde [693]. OPA showed good activity against the mycobacteria tested, including the glutaraldehyde-resistant strains, but 0.5% OPA was not sporicidal with 270 minutes of exposure. Increasing the pH from its unadjusted level (about 6.5) to pH 8 improved the sporicidal activity of OPA [694]. The level of biocidal activity was directly related to the temperature. A greater

than 5-$\log_{10}$ reduction of *B. atrophaeus* spores was observed in 3 hours at 35°C, than in 24 hours at 20°C. Also, with an exposure time ≤5 minutes, biocidal activity decreased with increasing serum concentration. However, efficacy did not differ when the exposure time was ≥10 minutes [697]. In addition, OPA is effective (>5-$\log_{10}$ reduction) against a wide range of microorganisms, including glutaraldehyde-resistant mycobacteria and *B. atrophaeus* spores [694].

The influence of laboratory adaptation of test strains, such as *P. aeruginosa*, to 0.55% OPA has been evaluated. Resistant and multiresistant strains increased substantially in susceptibility to OPA after laboratory adaptation ($\log_{10}$ reduction factors increased by 0.54 and 0.91 for resistant and multiresistant strains, respectively) [704]. Other studies have found naturally occurring cells of *P. aeurginosa* were more resistant to a variety of disinfectants than were subcultured cells [705].

Uses

OPA has several potential advantages over glutaraldehyde. It has excellent stability over a wide pH range (pH 3–9), is not a known irritant to the eyes and nasal passages [706], does not require exposure monitoring, has a barely perceptible odor, and requires no activation. OPA, like glutaraldehyde, has excellent material compatibility. A potential disadvantage of OPA is that it stains proteins gray (including unprotected skin) and thus must be handled with caution [69]. However, skin staining would indicate improper handling that requires additional training and/or personal protective equipment (e.g., gloves, eye and mouth protection, and fluid-resistant gowns). OPA residues remaining on inadequately water-rinsed transesophageal echo probes can stain the patient's mouth [707]. Meticulous cleaning, using the correct OPA exposure time (e.g., 12 minutes) and copious rinsing of the probe with water should eliminate this problem. The results of one study provided a basis for a recommendation that rinsing of instruments disinfected with OPA will require at least 250 mL of water per channel to reduce the chemical residue to a level that will not compromise patient or staff safety (<1 ppm) [708]. Personal protective equipment should be worn when contaminated instruments, equipment, and chemicals are handled [400]. In addition, equipment must be thoroughly rinsed to prevent discoloration of a patient's skin or mucous membrane.

In April 2004, the manufacturer of OPA disseminated information to users about patients who reportedly experienced an anaphylaxis-like reaction after cystoscopy where the scope had been reprocessed using OPA. Of approximately 1 million urologic procedures performed using instruments reprocessed using OPA, 24 cases (17 cases in the United States, six in Japan, one in the United Kingdom) of anaphylaxis-like reactions have been reported after repeated cystoscopy (typically after four to nine treatments). Preventive measures include removal of OPA residues by thorough rinsing and not using OPA for reprocessing urologic instrumentation used to treat patients with a history of bladder cancer (Nevine Erian, personal communication, June 4, 2004; Product Notification, Advanced Sterilization Products, April 23, 2004) [709].

A few OPA clinical studies are available. In a clinical-use study, OPA exposure of 100 endoscopes for 5 minutes resulted in a >5-$\log_{10}$ reduction in bacterial load. Furthermore, OPA was effective over a 14-day use cycle [100]. Manufacturer data show that OPA will last longer in an automatic endoscope reprocessor before reaching its MEC limit (MEC after 82 cycles) than will glutaraldehyde (MEC after 40 cycles) [400]. High-pressure liquid chromatography confirmed that OPA levels are maintained above 0.3% for at least 50 cycles [706, 710]. OPA must be disposed in accordance with local and state regulations. If OPA disposal through the sanitary sewer system is restricted, glycine (25 grams/gallon) can be used to neutralize the OPA and make it safe for disposal.

The high-level disinfectant label claims for OPA solution at 20°C vary worldwide (e.g., 5 minutes in Europe, Asia, and Latin America; 10 minutes in Canada and Australia; and 12 minutes in the United States). These label claims differ worldwide because of differences in the test methodology and requirements for licensure. In an automated endoscope reprocessor with an FDA-cleared capability to maintain solution temperatures at 25°C, the contact time for OPA is 5 minutes.

Peracetic Acid

Overview

Peracetic, or peroxyacetic, acid is characterized by rapid action against all microorganisms. Special advantages of peracetic acid are that it lacks harmful decomposition products (i.e., acetic acid, water, oxygen, hydrogen peroxide), enhances removal of organic material [711], and leaves no residue. It remains effective in the presence of organic matter and is sporicidal even at low temperatures (Tables 4 and 5). Peracetic acid can corrode copper, brass, bronze, plain steel, and galvanized iron but these effects can be reduced by additives and pH modifications. It is considered unstable, particularly when diluted; for example, a 1% solution loses half its strength through hydrolysis in 6 days, whereas 40% peracetic acid loses 1%–2% of its active ingredients per month [654].

Mode of Action

Little is known about the mechanism of action of peracetic acid, but it is believed to function similarly to other oxidizing agents—that is, it denatures proteins, disrupts the cell wall permeability, and oxidizes sulfhydryl and sulfur bonds in proteins, enzymes, and other metabolites [654].

Microbicidal Activity

Peracetic acid will inactivate gram-positive and gram-negative bacteria, fungi, and yeasts in ≤5 minutes at <100 ppm. In the presence of organic matter, 200–500 ppm is required. For viruses, the dosage range is wide (12–2250 ppm), with poliovirus inactivated in yeast extract in 15 minutes with 1,500–2,250 ppm. In one study, 3.5% peracetic acid was ineffective against HAV after 1-minute exposure using a carrier test [58]. Peracetic acid (0.26%) was effective (log_{10} reduction factor >5) against all test strains of mycobacteria (*M. tuberculosis, M. avium-intracellulare, M. chelonae, and M. fortuitum*) within 20–30 minutes in the presence or absence of an organic load [607, 712]. With bacterial spores, 500–10,000 ppm (0.05%–1%) inactivates spores in 15 seconds to 30 minutes using a spore suspension test [654, 659, 713-715].

Uses

An automated machine using peracetic acid to chemically sterilize medical (e.g., endoscopes, arthroscopes), surgical, and dental instruments is used in the United States[716-718]. As previously noted, dental handpieces should be steam sterilized. The sterilant, 35% peracetic acid, is diluted to 0.2% with filtered water at 50°C. Simulated-use trials have demonstrated excellent microbicidal activity [111, 718-722], and three clinical trials have demonstrated both excellent microbial killing and no clinical failures leading to infection[90, 723, 724]. The high efficacy of the system was demonstrated in a comparison of the efficacies of the system with that of ethylene oxide. Only the peracetic acid system completely killed 6 log_{10} of *M. chelonae, E. faecalis,* and *B. atrophaeus* spores with both an organic and inorganic challenge[722]. An investigation that compared the costs, performance, and maintenance of urologic endoscopic equipment processed by high-level disinfection (with glutaraldehyde) with those of the peracetic acid system reported no clinical differences between the two systems. However, the use of this system led to higher costs than the high-level disinfection, including costs for processing ($6.11 vs. $0.45 per cycle), purchasing and training ($24,845 vs. $16), installation ($5,800 vs. $0), and endoscope repairs ($6,037 vs. $445) [90]. Furthermore, three clusters of infection using the peracetic acid automated endoscope reprocessor were linked to inadequately processed bronchoscopes when inappropriate channel connectors were used with the system [725]. These clusters highlight the importance of training, proper model-specific endoscope connector systems, and quality-control procedures to ensure compliance with endoscope manufacturer recommendations and professional organization guidelines. An alternative high-level disinfectant available in the United Kingdom contains 0.35% peracetic acid. Although this product is rapidly effective against a broad range of microorganisms [466, 726, 727], it tarnishes the metal of endoscopes and is unstable, resulting in only a 24-hour use life [727].

Peracetic Acid and Hydrogen Peroxide

Overview

Two chemical sterilants are available that contain peracetic acid plus hydrogen peroxide (i.e., 0.08% peracetic acid plus 1.0% hydrogen peroxide [no longer marketed]; and 0.23% peracetic acid plus 7.35% hydrogen peroxide (Tables 4 and 5).

Microbicidal Activity

The bactericidal properties of peracetic acid and hydrogen peroxide have been demonstrated [728]. Manufacturer data demonstrated this combination of peracetic acid and hydrogen peroxide inactivated all microorganisms except bacterial spores within 20 minutes. The 0.08% peracetic acid plus 1.0% hydrogen peroxide product effectively inactivated glutaraldehyde-resistant mycobacteria[729].

Uses

The combination of peracetic acid and hydrogen peroxide has been used for disinfecting hemodialyzers [730]. The percentage of dialysis centers using a peracetic acid-hydrogen peroxide-based disinfectant for reprocessing dialyzers increased from 5% in 1983 to 56% in 1997[249]. Olympus America does not endorse use of 0.08% peracetic acid plus 1.0% hydrogen peroxide (Olympus America, personal communication, April 15, 1998) on any Olympus endoscope because of cosmetic and functional damage and will not assume liability for chemical damage resulting from use of this product. This product is not currently available. FDA has cleared a newer chemical sterilant with 0.23% peracetic acid and 7.35% hydrogen peroxide (Tables 4 and 5). After testing the 7.35% hydrogen peroxide and 0.23% peracetic acid product, Olympus America concluded it was not compatible with the company's flexible gastrointestinal endoscopes; this conclusion was based on immersion studies where the test insertion tubes had failed because of swelling and loosening of the black polymer layer of the tube (Olympus America, personal communication, September 13, 2000).

Phenolics

Overview

Phenol has occupied a prominent place in the field of hospital disinfection since its initial use as a germicide by Lister in his pioneering work on antiseptic surgery. In the past 30 years, however, work has concentrated on the numerous phenol derivatives or phenolics and their antimicrobial properties. Phenol derivatives originate when a functional group (e.g., alkyl, phenyl, benzyl, halogen) replaces one of the hydrogen atoms on the aromatic ring. Two phenol derivatives commonly found as constituents of hospital disinfectants are *ortho*-phenylphenol and *ortho*-benzyl-*para*-chlorophenol. The antimicrobial properties of these compounds and many other phenol derivatives are much improved over those of the parent chemical. Phenolics are absorbed by porous materials, and the residual disinfectant can irritate tissue. In 1970, depigmentation of the skin was reported to be caused by phenolic germicidal detergents containing *para*-tertiary butylphenol and *para*-tertiary amylphenol [731].

Mode of Action

In high concentrations, phenol acts as a gross protoplasmic poison, penetrating and disrupting the cell wall and precipitating the cell proteins. Low concentrations of phenol and higher molecular-weight phenol derivatives cause bacterial death by inactivation of essential enzyme systems and leakage of essential metabolites from the cell wall [732].

Microbicidal Activity

Published reports on the antimicrobial efficacy of commonly used phenolics showed they were bactericidal, fungicidal, virucidal, and tuberculocidal [14, 61, 71, 73, 227, 416, 573, 732-738]. One study demonstrated little or no virucidal effect of a phenolic against coxsackie B4, echovirus 11, and poliovirus 1 [736]. Similarly, 12% *ortho*-phenylphenol failed to inactivate any of the three hydrophilic viruses after a 10-minute exposure time, although 5% phenol was lethal for these viruses [72]. A 0.5% dilution of a phenolic (2.8% *ortho*-phenylphenol and 2.7% *ortho*-benzyl-*para*-chlorophenol) inactivated HIV [227] and a 2% solution of a phenolic (15% ortho-phenylphenol and 6.3% para-tertiary-amylphenol) inactivated all but one of 11 fungi tested [71].

Manufacturers' data using the standardized AOAC methods demonstrate that commercial phenolics are not sporicidal but are tuberculocidal, fungicidal, virucidal, and bactericidal at their recommended use-dilution. Attempts to substantiate the bactericidal label claims of phenolics using the AOAC Use-Dilution Method occasionally have failed [416, 737]. However, results from these same studies have varied dramatically among laboratories testing identical products.

Uses

Many phenolic germicides are EPA-registered as disinfectants for use on environmental surfaces (e.g., bedside tables, bedrails, and laboratory surfaces) and noncritical medical devices. Phenolics are not FDA-cleared as high-level disinfectants for use with semicritical items but could be used to preclean or decontaminate critical and semicritical devices before terminal sterilization or high-level disinfection.

The use of phenolics in nurseries has been questioned because of hyperbilirubinemia in infants placed in bassinets where phenolic detergents were used [739]. In addition, bilirubin levels were reported to increase in phenolic-exposed infants, compared with nonphenolic-exposed infants, when the phenolic was prepared according to the manufacturers' recommended dilution [740]. If phenolics are used to clean nursery floors, they must be diluted as recommended on the product label. Phenolics (and other disinfectants) should not be used to clean infant bassinets and incubators while occupied. If phenolics are used to terminally clean infant bassinets and incubators, the surfaces should be rinsed thoroughly with water and dried before reuse of infant bassinets and incubators [17].

Quaternary Ammonium Compounds

Overview

The quaternary ammonium compounds are widely used as disinfectants. Health-care–associated infections have been reported from contaminated quaternary ammonium compounds used to disinfect patient-care supplies or equipment, such as cystoscopes or cardiac catheters [741, 742]. The quaternaries are good cleaning agents, but high water hardness [743] and materials such as cotton and gauze pads can make them less microbicidal because of insoluble precipitates or cotton and gauze pads absorb the active ingredients, respectively. One study showed a significant decline (~40%–50% lower at 1 hour) in the concentration of quaternaries released when cotton rags or cellulose-based wipers were used in the open-bucket system, compared with the nonwoven spunlace wipers in the closed-bucket system.[744] As with several other disinfectants (e.g., phenolics, iodophors) gram-negative bacteria can survive or grow in them [404].

Chemically, the quaternaries are organically substituted ammonium compounds in which the nitrogen atom has a valence of 5, four of the substituent radicals (R1-R4) are alkyl or heterocyclic radicals of a given size or chain length, and the fifth (X^-) is a halide, sulfate, or similar radical [745]. Each compound exhibits its own antimicrobial characteristics, hence the search for one compound with outstanding antimicrobial properties. Some of the chemical names of quaternary ammonium compounds used in healthcare are alkyl dimethyl benzyl ammonium chloride, alkyl didecyl dimethyl ammonium chloride, and dialkyl dimethyl ammonium chloride. The newer quaternary ammonium compounds (i.e., fourth

generation), referred to as twin-chain or dialkyl quaternaries (e.g. didecyl dimethyl ammonium bromide and dioctyl dimethyl ammonium bromide), purportedly remain active in hard water and are tolerant of anionic residues [746].

A few case reports have documented occupational asthma as a result of exposure to benzalkonium chloride [747].

Mode of Action

The bactericidal action of the quaternaries has been attributed to the inactivation of energy-producing enzymes, denaturation of essential cell proteins, and disruption of the cell membrane[746]. Evidence exists that supports these and other possibilities [745 748].

Microbicidal Activity

Results from manufacturers' data sheets and from published scientific literature indicate that the quaternaries sold as hospital disinfectants are generally fungicidal, bactericidal, and virucidal against lipophilic (enveloped) viruses; they are not sporicidal and generally not tuberculocidal or virucidal against hydrophilic (nonenveloped) viruses[14, 54-56, 58, 59, 61, 71, 73, 186, 297, 748, 749]. The poor mycobactericidal activities of quaternary ammonium compounds have been demonstrated [55, 73]. Quaternary ammonium compounds (as well as 70% isopropyl alcohol, phenolic, and a chlorine-containing wipe [80 ppm]) effectively (>95%) remove and/or inactivate contaminants (i.e., multidrug-resistant *S. aureus*, vancomycin-resistant *Entercoccus*, *P. aeruginosa*) from computer keyboards with a 5-second application time. No functional damage or cosmetic changes occurred to the computer keyboards after 300 applications of the disinfectants [45].

Attempts to reproduce the manufacturers' bactericidal and tuberculocidal claims using the AOAC tests with a limited number of quaternary ammonium compounds occasionally have failed [73, 416, 737]. However, test results have varied extensively among laboratories testing identical products [416, 737].

Uses

The quaternaries commonly are used in ordinary environmental sanitation of noncritical surfaces, such as floors, furniture, and walls. EPA-registered quaternary ammonium compounds are appropriate to use for disinfecting medical equipment that contacts intact skin (e.g., blood pressure cuffs).

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