

Chemical disinfectants in ophthalmic practice

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The instrumentation used in ophthalmic clinics can be a source of epidemics in health care set up. Contact tonometry with Schiottz or Applanation tonometer is associated with nosocomial epidemic keratoconjunctivitis outbreaks. Recently identified SARS-CoV-2 (COVID -19) spreads mainly via the respiratory route and fomites and can transmit through other body fluids, including tear film. Various ophthalmic instruments can become a common source of spreading cross infections. Chemical disinfection is one of the most common methods employed to decontaminate instruments and environmental surfaces and prevent transmission of infectious pathogens to patients through medical and surgical instruments. Various chemical disinfectants are available with a varied spectrum to work on a different group of organisms. In this article, we briefly cover commonly used chemical disinfectants in ophthalmic practice like Alcohol (Ethyl Alcohol, Isopropyl Alcohol), Chlorine-based solution (mainly Sodium Hypochlorite), Glutaraldehyde, Hydrogen Peroxide, Formaldehyde, Iodophors, and Quaternary Ammonium Compounds

Key words: Chemical disinfectants, glutaraldehyde, isopropyl alcohol, ophthalmic practice, sodium hypochlorite

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The instrumentation used in the outpatient department (OPD) and operation theatres can be a source of an epidemic in health care set up. Contact tonometry with Schiottz or applanation tonometer is a known risk factor for epidemic keratoconjunctivitis (EKC) and also linked to nosocomial EKC outbreaks.^[1,2] other specialties have also documented similar incidences of nosocomial infection via instruments.^[3,4] Failure to properly disinfect or sterilize equipment carries the risk for person-to-person transmission (e.g., hepatitis B virus) and transmission of environmental pathogens (e.g., *Pseudomonas aeruginosa*).

We must understand the difference between sterilant and disinfectant, the terminologies used routinely and flexibly

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in practice. 'Sterilization' refers to a physical or chemical process that destroys or removes all microbial life, including spores.^[5] Unlike sterilization, disinfection is not sporicidal. A few disinfectants can kill spores with prolonged exposure times (3–12 h); these are called 'chemical sterilants'.^[5] At similar concentrations but with shorter exposure periods (e.g., 20 min for 2% glutaraldehyde), these same disinfectants can kill all microorganisms except large numbers of bacterial spores; they are called high-level disinfectants.^[5] Low-level disinfectants can kill most vegetative bacteria, fungi, and some viruses in a reasonable time (≤ 10 min). Prior cleaning of the object; the presence of organic and inorganic load; type and level of microbial contamination; concentration of and exposure time to the disinfectant; physical nature of the object (e.g., crevices, hinges, and lumens); temperature and pH of the disinfection process affects the efficacy of both disinfection and sterilization.^[5]

SARS-CoV-2, the virus linked to the current pandemic, is an enveloped virus with an extraordinarily large single-stranded RNA genome ranging from 26 to 32 kilobases in length. It has a fragile outer lipid envelope that makes it more susceptible to disinfectants and heat than non-enveloped viruses such as Rotavirus, Norovirus, and Poliovirus.^[6] It has already affected nearly 200 countries and territories.^[7] This virus spreads mainly via respiratory route and fomites; reports also suggest conjunctivitis as one spectrum of its presentation and a high probability of virus being present in the body fluids including tear film.^[8,9]

Recently, AIOS-IJO Consensus statement and AIOS guidelines suggested incongruent concentrations of sodium hypochlorite (1% & 0.5% respectively) for sterilization of

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various ophthalmic instruments in OPD.^[10,11] Variability in guidelines may create ambiguity and apprehension among ophthalmologists. In the unacquainted pandemic, it is a physician's onus to prevent the spread of this virus through instruments from patient to patient. This article attempts to re-visit commonly used disinfectants in ophthalmic practice, which may formulate an evidence-based approach towards the use of chemical disinfectants. Table 1 lists frequently used chemical disinfectants in ophthalmic practice.

Alcohol

Ethyl Alcohol and Isopropyl Alcohol are commonly used solutions in the healthcare industry. Their cidal activity declines sharply below the dilution of 50% concentration, and the optimum bactericidal concentration is 60%–90% solutions in water (volume/volume). Its antimicrobial action is due to the denaturation of proteins. Its bacteriostatic effect is due to the inhibition of the production of metabolites essential for rapid cell division.^[12] 60%–80% concentration of Ethyl alcohol is a potent virucidal agent that can inactivate all of the lipophilic viruses (e.g., Corona viridae, Herpes, Vaccinia, and Influenza) and many hydrophilic viruses (Adenovirus, Rotavirus). Isopropyl alcohol is not active against the non-lipid enteroviruses like Adenovirus but is active against the lipid viruses (e.g., Coronavirus group).^[13-15] Alcohols based disinfectants can be used effectively for sterilization of various health care instrumentation.^[17-19] Isopropyl Alcohol Swabs are used to disinfect Goldmann Applanation tips/Goniolenses/other non-contact lenses. However, the alcohol-based solution can 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,^[20] and damage tonometer tips (by the deterioration of the glue) after the equivalent of 1 working year of routine use.^[21] Tonometer biprisms soaked in alcohol for four days developed rough front surfaces that potentially could cause corneal damage.^[22] Corneal opacification is reported if IOP is measured immediately after cleaning tonometer tips with alcohol.^[23] Alcohols are flammable and consequently must be stored in a cool, well-ventilated area. Food and Drug Administration of the United States of America (USFDA) does not approve Alcohol-based solutions as a chemical sterilant or high-level disinfectant.

Commonly used commercially available Alcohol products containing Ethyl Alcohol are Sterlium and Hexiprep-T, and those containing Isopropyl alcohol are BD Swab and Sterlmax.

Chlorine and Chlorine Compounds

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 are aqueous solutions of 5.25%–6.15% sodium hypochlorite, 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.^[24] Sodium hypochlorite at the concentration used in household bleach (5.25%–6.15%) can produce ocular irritation or oropharyngeal, esophageal, and gastric burns and chemical corneal injury.^[25-29] It is corrosive to metals in high concentrations. The microbicidal activity of chlorine is attributed mostly to undissociated hypochlorous acid (HOCl). 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 one month.^[30]

The microbicidal mechanism of chlorine involves a combination of factors like ring chlorination of amino acids, loss of intracellular contents, decreased uptake of nutrients, inhibition of protein synthesis, decreased oxygen uptake, breaks in DNA, and depressed DNA synthesis leading to protein inhibition.^[31,32] Sodium Hypochlorite is bactericidal at 25 ppm (0.025%), fungicidal at 0.02% (200 ppm), sporicidal and mycobactericidal at 1000 ppm (0.1%), virucidal at 200 to 500 ppm (0.02%–0.05%).^[13,31,33-34] It is effective against both lipophilic (including HIV) and hydrophilic groups of viruses.^[35] Sterilization of applanation tip and spot-disinfection of countertops and floors can be done by 0.1% to 0.5% freshly prepared solution of Sodium Hypochlorite.^[36-39] However, one must remember that 0.5% solution of Sodium Hypochlorite is corrosive and reduces the prism life to maximum 100 cycles of 1 h each.^[40] 0.5% solution of Sodium Hypochlorite is recommended only for high contamination or large spills of blood and body fluids (>10 mL).^[41]

Alternative compounds that release chlorine and used in the healthcare setting include:

- Demand-release chlorine dioxide
- Sodium dichloroisocyanurate
- Chloramine-T
- Superoxidized water.

The advantage of these compounds over the hypochlorites is that they retain chlorine longer and hence exert a bactericidal effect, and USFDA has approved them as a high-level disinfectant. However, we require specialized equipment to produce the super-oxidized water with perfect parameters such as pH, current, and redox potential. Super-oxidized water should have a pH of 5.5–7.0 and an oxidation-reduction potential (redox) of >900 mV." We need to prepare it fresh as its effectivity reduces with time.^[42-44]

Commonly used commercially available products in India are Dakin's Solution (Sodium Hypochlorite 0.25% & 0.5%) and Hypocin Eyelid Cleaner (Super-oxidized solution).

Glutaraldehyde

Glutaraldehyde is a saturated dialdehyde. The antimicrobial activity of the solution depends on the duration of dilution, its concentration, and organic stress. Its alkaline solution is sporicidal. The biocidal activity of glutaraldehyde results from alkylation of sulfhydryl, hydroxyl, carboxyl, and amino groups of microorganisms, which alters RNA, DNA, and protein synthesis.^[45,46] ≥2% aqueous solutions of Glutaraldehyde, buffered to pH 7.5–8.5 with sodium bicarbonate is bactericidal in less than 2 min; mycobactericidal, fungicidal, virucidal in <10 min; and sporicidal in 3 h.^[45-50] It is effective against both lipophilic and hydrophilic groups of viruses. A solution of 2.4% and 3.4% glutaraldehyde and combined solution of 1.12% glutaraldehyde with a 1.93% phenol/phenate is approved as a high-level disinfectant. Glutaraldehyde is non-corrosive and commonly used as a high-level disinfectant for medical equipment such as endoscopes, anesthesia equipment, and various medical instruments.^[50-55] Bacillocid Special Solution, which contains Glutaraldehyde, can be used to clean Goldmann Applanation tips and Goniolenses. Once diluted, this solution has a shelf-life of minimally 14 days.^[55] As it is toxic and expensive, it should be avoided for cleaning of non-critical surfaces. If equipment's processing is done in poorly ventilated rooms, healthcare personnel can be exposed to high levels of glutaraldehyde vapor.^[49] Acute or chronic exposure can result in skin irritation or dermatitis, mucous membrane irritation (eye, nose, mouth), epistaxis, allergic contact dermatitis, asthma, and rhinitis.^[56-59]

Table 1: Summarizes commonly used Chemical disinfectants in ophthalmic practice with their known mechanism of action, microbicidal activity, common side effects, and special instructions

No	Disinfectant	Mechanism of Action	Microbicidal Activity (Concentration Required)	Dilution, diluent	Common Side Effects	Comments
1	Alcohol					
1a	Ethyl Alcohol	Denaturation of proteins	Bactericidal (60-95%): Gram +ve, Gram -ve Mycobactericidal (95%) Virucidal (Liphophilic & Hydrophilic): 60-80% Fungicidal: 70%	No need for dilution		Cidal activity drops at a concentration below 50% Lacks sporicidal action
1b	Isopropyl Alcohol	Denaturation of proteins	Bactericidal (70%): Gram+ve, Gram -ve Mycobactericidal; 70% Virucidal (Lipophilic): 70% Fungicidal: 70%	No need for dilution	Damage to tonometer biprism Damage to shellac mountings of lensed instrument	Cidal activity drops at a concentration below 50% Lacks sporicidal action
2	Chlorine and Chlorine Compounds Sodium Hypochlorite	Loss of intracellular contents Decreased uptake of nutrients Inhibition of protein synthesis	Bactericidal at a minimal concentration of 25 ppm (0.0025%) Mycobactericidal at a minimal concentration of 1000 ppm (0.1%) Virucidal at a minimal concentration of 200-500 ppm (0.02-0.05%) Fungicidal at a minimal concentration of 500 ppm (0.05%) Sporicidal at a minimal concentration of 1000 ppm (0.1%)	Dilute with cold water, amount of diluent based on % bleach and % diluted hypochlorite required	Corrosion of applanation tips at $\geq 0.5\%$ (≥ 5000 ppm) Ocular irritation or Oropharyngeal Esophageal, and Gastric burns	
3	Glutaraldehyde	Alters RNA, DNA, and protein synthesis	Bactericidal Fungicidal Virucidal Sporicidal (Alkaline solution) Mycobactericidal	No need for dilution	Skin irritation or Dermatitis, Mucous membrane irritation (eye, nose, mouth)	Available as Bacillocid Special (the combination of 1, 6 Dihydroxy 2,5-dioxyhexane 11.2%, Glutaraldehyde 5%, Benzalkonium chloride 5% and Alkyl Urea Derivative 3% Need to dilute to make 2% solution Non-corrosive to metals Does not damage the lens instrument, rubber, plastics
4	Hydrogen Peroxide	Attacks membrane lipids, DNA and other essential cell components	Bactericidal in 1 min Virucidal in 1 min	No need for dilution	Corneal damage	Stable when properly stored (e.g., in dark containers)

Contd...

Table 1: Contd...

No	Disinfectant	Mechanism of Action	Microbicidal Activity (Concentration Required)	Dilution, diluent	Common Side Effects	Comments
			Sporicidal in 6 h Fungicidal in 5 min Mycobactericidal in 20 min			
5	Iodophores	Disruption of Protein and Nucleic acid structure and synthesis	Bactericidal Fungicidal Virucidal Sporicidal Mycobactericidal	No need for dilution		Commonly used as Anti-septic and Disinfectant. Unsuitable for hard surface disinfection
6	Formaldehyde	Alkylating the Amino and Sulfhydryl groups of proteins and ring nitrogen atoms of Purine bases	Bactericidal Fungicidal Virucidal Sporicidal Mycobactericidal	Room temperature water in 1: 2 ratio of formalin to water	Releases Irritating fumes and Pungent odor even at very low levels (<1 ppm) Carcinogenic	
7	Quaternary Ammonium Compounds	Inactivation of energy-producing enzymes, denaturation of essential cell proteins, and disruption of the cell membrane	Fungicidal Bactericidal Virucidal against lipophilic (enveloped) viruses	No need for dilution		Less corrosive compared to sodium hypochlorite Not effective against hydrophilic (non-enveloped) viruses

Commonly used commercially available products are Bacilloid Extra and Glutaraldehyde solution 2.45% by Glutradex.

Formaldehyde

Formaldehyde is used principally as a water-based solution called formalin, which is 37% formaldehyde by weight. The aqueous solution is bactericidal, mycobactericidal, fungicidal, virucidal, and sporicidal.^[13,60-62] It is a potential carcinogen, and standard should be set, limiting employee's exposure time to formaldehyde as per standard guidelines.^[63] It inactivates microorganisms by alkylating the amino and sulfhydryl groups of proteins and ring nitrogen atoms of purine bases.^[64] It destroys a wide range of microorganisms at varying concentrations. It is virucidal at 2% except poliovirus requires 8% concentration,^[13] mycobactericidal at 4%,^[60] and bactericidal at 2.5%.^[62] The sporicidal action of formaldehyde is slow and takes at least 2 h compared to only 15 min with Glutaraldehyde. Although formaldehyde-alcohol is a high-level disinfectant, its healthcare uses are limited by irritating fumes and pungent odor even at very low levels (<1 ppm). It mainly used as Fumigator in Operation Theater.

Commonly used commercially available products in India are Microtroniks Formaldehyde Solution (37-41% Formalin Solutions) and Daffodil's Formalin Solution (37%-41% W/V).

Hydrogen Peroxide

Stabilized Hydrogen Peroxide is extensively used in health care set up and has got approval as a high-level disinfectant. Concentrations of hydrogen peroxide from 6% to 25% show promise as chemical sterilants. It works

by producing destructive hydroxyl free radicals that can attack membrane lipids, DNA, and other essential cell components. Organisms that possess cytochrome systems can protect cells by degrading hydrogen peroxide to water and oxygen.^[65,66] It has bactericidal, virucidal, sporicidal, and fungicidal properties.^[65,66] However, it has limited action against hydrophilic viruses (e.g., Adenovirus). Concentrations ranging from 3% to 6% are used to disinfect soft contact lenses (e.g., 3% for 2-3 hrs)^[58,67,68] tonometer biprisms,^[22] and endoscopes.^[65-68] Improperly rinsed applanation tip prism can cause corneal damage.^[69] 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%). Hydrogen peroxide is exceptionally stable when stored in dark containers.

Commonly used commercially available products in India are Clorox Healthcare Hydrogen Peroxide and Hydrogen Peroxide 3% by National Peroxide Ltd.

Iodophors

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. Iodine can quickly penetrate the cell wall of microorganisms and disrupt the synthesis of protein and nucleic acid. Iodophors are bactericidal, mycobactericidal, and virucidal but require prolonged contact times to kill certain fungi and bacterial spores.^[33,70,71] Most commercially available iodophors are not sporicidal at their recommended use-dilution. Its use

Table 2: Summarizes the suggested uses of the chemical disinfectants in ophthalmic OPD

No	Disinfectant	Desired concentration	Ophthalmic uses	Dilution, diluent	Commercially available products
1	Alcohol				
1a	Ethyl Alcohol	60% to 95%	Hand disinfectant, Hard surface, Tabletops, Doorknobs, Chair unit, Trial frame Hard surface (headrest, chin rest, joystick, etc.) of machines like OCT, HVF and Slit-lamp parts except oculars	No need for dilution	Sterillium Hexiprep-T
1b	Isopropyl Alcohol	70%	Applanation tip, Goniolenses Probes (A-scan, B-scan, Pachymetry, UBM)	No need for dilution	BD Alcohol swab Sterlomax
2	Chlorine and Chlorine Compounds Sodium Hypochlorite	0.10%	Applanation tip, Goniolenses	Dilute with cold water in 5:1 ratio to make a 0.1% solution	Dakin Solution (0.5%)
		0.50%	Hard surfaces, Tabletops, Doorknobs	No need for dilution	Hypocin Eyelid Cleaner (Super Oxidized solution)
3	Glutaraldehyde	2%	Applanation tip, Goniolenses Probes (A-scan, B-scan, Pachymetry, UBM) Hard surfaces (headrest, chin rest, joystick etc.) of Machines like OCT, HVF Slit-lamp parts except for oculars Endoscopes	Dilute with cold water in 2.5:1 ratio to make 2% solution No need for dilution	Bacillocid Extra Glutaraldehyde solution 2.45% by Glutradex
4	Hydrogen Peroxide	3%	Applanation tip Endoscopes	No need for dilution	Clorox Healthcare Hydrogen Peroxide Hydrogen Peroxide 3% by National Peroxide Ltd
5	Iodophores		Pre-operative preparation Pre-operative scrubbing	No need for dilution	Betadine Wokadine 5% Solution
6	Formaldehyde	37%	Fumigation	Water in 2:1 ratio of formalin to water	Microtroniks Formaldehyde Solution 37-41% Formalin Solutions Daffodil's Formalin Solution (37-41% W/V)
7	Quaternary Ammonium Compounds		Environmental sanitation of non-critical surfaces, such as floors, furniture, and walls. disinfecting equipment that contacts intact skin (trial frame)	No need for dilution No need for dilution No need for dilution	D-125: From Microgen D-256: From Microgen Ammdent Glutapex Cleaner

in Ophthalmology is limited to pre-operative cleaning of the surgical site and disinfecting medical instruments and endoscopes. They are not suitable for disinfecting hard surfaces. USFDA has not cleared any liquid chemical sterilant or high-level disinfectants with iodophors as the main active ingredient.

Commonly used commercially available products in India are BETADINE* 5% Sterile Ophthalmic Prep Solution and Wokadine 5% Solution.

Quaternary Ammonium Compounds

The quaternary ammonium compounds are commonly used disinfectants. Their activity reduces in hard water; however, the newer quaternary ammonium compounds referred to dialkyl quaternary (e.g., didecyl dimethyl ammonium bromide) remain active in hard water.^[44] It causes inactivation of energy-producing enzymes, denaturation of essential cell proteins, and disruption of the cell membrane. It is fungicidal, bactericidal, and virucidal against lipophilic (enveloped)

viruses but ineffective against hydrophilic (nonenveloped) viruses.^[44] This compound is less corrosive compared to sodium hypochlorite. Its use is common in environmental sanitation of non-critical surfaces, such as floors, furniture, and walls. It can also be used for disinfecting medical equipment that contacts intact skin (e.g., trial frame).

Commonly used commercially available products in India are D-125 (3rd generation twin chain quaternary ammonium compound), D-256 (5th generation twin chain quaternary ammonium compound) from Microgen.

Table 1 summarizes commonly used Chemical disinfectants in ophthalmic practice with their known mechanism of action, microbicidal activity, common side effects, and special instructions. Table 2 summarizes the suggested uses of the chemical disinfectants in ophthalmic OPD with the most commonly available commercial products.

Conclusion

To conclude, we need to address the issues of cross-infection and the spread of the SARS-CoV-2 virus. As physicians, we have the onus to prevent or minimize the risk of spreading infection from patient to patient. As everyone is naïve to this pandemic, it becomes difficult to decide the type of disinfectant to choose from the current armamentarium of disinfectants. Proper knowledge of all available chemical disinfectants may help us in our decision making, and by making minor changes in our current protocols of disinfection, we shall be able to keep patients and ourselves on a safer side.

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Conflicts of interest

There are no conflicts of interest.

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