

تفريغ تعقيم



(3)

محاضرة:

الصيدلانية: عروب طرابلس



لجان التفتحات



Chemical disinfectants, antiseptics and preservatives

Chapter 19

Definitions

- ▶ Disinfection: the process of removing MOs, including pathogens, from the surface of inanimate objects
- ▶ Chemical disinfectants are capable of different levels of action:

تادرسه صو يايح رختلفه يي الويل

Table 19.1 Levels of disinfection attainable when products are used according to manufacturer's instructions تکلیف يي ايشاره ا هصنه

	<u>Low</u>	Disinfection level <u>Intermediate</u>	<u>High</u>
<u>Microorganisms killed</u>	<u>Most vegetative bacteria</u> <u>Some viruses</u> <u>Some fungi</u>	<u>Vegetative bacteria including M. tuberculosis</u> <u>Most viruses including hepatitis B virus (HBV), Most fungi</u>	<u>All microorganisms unless extreme challenge or resistance exhibited</u>
<u>Microorganisms surviving</u>	<u>M. tuberculosis</u> <u>Bacterial spores prions</u>	<u>Bacterial spores</u> <u>Prions</u>	<u>Extreme challenge of resistant bacterial spores</u> <u>Prions</u>

Definitions

- ▶ Antisepsis: destruction or inhibition of MOs on living tissues having the effect of limiting or preventing the harmful results of infection منه النتائج الضارة. للمرض
 - ▶ Should be non toxic or irritating to mucous membranes and skin
 - ▶ Uses:
 - Reduce microbial population on the skin before surgery
 - On hands to help prevent spread of infection
-



Definitions

المبررات
الجامعة

①
②
Preservatives are included in pharmaceutical and many
type of formulations to prevent microbial spoilage of the
product:
القلق الميكروبي
للحد من انتشار

1. Non sterile products: to limit proliferation of MO that
may be introduced unavoidably into non-sterile
products such as oral and topical medications during
their manufacture and use
2. Sterile products (multi-use preparations): preservatives
should kill any microbial contaminants introduced
③ دون قصد inadvertently during use
3. Should be non toxic in relation to the intended route of
administration

Factors affecting choice of antimicrobial agents

تحدد استخدام العامل ذلك مظهر او ماديها فقط

1. Properties of chemical agent:

- Tissue toxicity: determine whether the agent can be used as an antiseptic or preservative

2. The type of MO and the levels of contamination:

Viruses, fungi, spores...etc

High bioburden → long exposure time and/or higher conc.

3. Intended application:

- The ingredients in preparations may antagonize preservative activity
- Risk to patient (break skin or introduced into sterile area of the body)
- Disinfectant should not corrode instrument, affect clarity of lenses

يعني عكس

يجب ان لا يتسبب بتآكل الاداة

او يؤثر على جودتها العدسات

Factors affecting choice of antimicrobial agents

4. Environmental factors:

- Bloody fluids, pus, ..
- Objects to be disinfected should be thoroughly cleaned (since dried organic deposits may inhibit penetration of the biocidal agent)
- Presence of ions (hard water)

لأن المواد السائلة الجافة
قد تمنع اختراق العامل المبيد
الحشري



Types of compound

Acids and esters

1. Benzoic acid:

- The non ionized acid is the active substance
- pK_a of benzoic acid = 4.2 (at this pH 50% of benzoic acid is ionized)
- It is advisable to limit use of acid to preservation of pharmaceuticals with a maximum of final pH of 5.0
- 0.05%-0.1% for oral preparations
- Benzoic acid + salicylic acid → used in the treatment of superficial fungal infections

2. Sorbic acid:

- pK_a = 4.8
- Gums, mucilages and syrups



Types of compound

Acids and esters

3. Esters of p-hydroxybenzoic acid (parabens):

- Alkyl esters of p-hydroxybenzoic acid
 - Developed to overcome the marked pH dependence on activity of the acids
 - pKa 8-8.5
 - Exhibit good preservative activity even at pH levels of 7-8
 - ^{تتغلب في} Active against a wide range of fungi but are less so against bacteria especially pseudomonas which may utilize them as carbon source
 - Frequently used as preservatives of emulsions, creams and lotions where two phases exists
-



Types of compound

Acids and esters

3. Esters of p-hydroxybenzoic acid (parabens)- continued:

- Combinations: the more water-soluble ester protects the aqueous phase, whereas the propyl or butyl esters give protection to the oil phase
- Limitation: inactivation of parabens occurs with non-ionic surfactants (care must be taken in formulation with both materials)



Types of compound

Alcohols

1. Alcohols used for disinfection and antiseptis:
 - Ethanol and isopropanol are used for disinfection and antiseptis
 - Bactericidal but not sporicidal
 - Cidal activity drops sharply below 50% concentration
 - Alcohols have poor penetration of organic matter and thus their use restricted to clean conditions
 - Widely used for skin preparation before injection or other surgical procedures
 - Alcohol hand-rub
-



Types of compound

Alcohols

- ▶ The presence of water is essential for activity of ethanol → 100% ethanol is relatively ineffective:
- 60-95% are bactericidal
- 70% is usually employed for the disinfection of skin, clean instruments or surfaces
- 90% ethanol is also active against fungi and most lipid-containing viruses including HIV
- Also ethanol a popular choice in pharmaceutical preparations and cosmetic products as a solvent and preservative

غير ضال



70% percent of alcohol is ideal to a stronger solution. Pure alcohol coagulates protein in contact. Suppose the pure alcohol is poured over a single celled organism. The alcohol will go through the cell wall of the organism in all direction, coagulating the protein just inside the cell wall. The ring of the coagulated protein would then stop the alcohol from penetrating farther from the cell, and no more coagulation would take place. At this time the cell would become inactive but not dead. Under the favorable conditions the cell would then begin to function. If 70 percent of alcohol is poured to a single celled organism, the diluted alcohol also coagulates the protein, but at a slower rate, so that it penetrates all the way through the cell before coagulation can block it. Then the entire cell is coagulated and the organism dies. Why is 70% ethanol used for wiping microbiological working areas? - ResearchGate. Available from:

https://www.researchgate.net/post/Why_is_70_ethanol_used_for_wiping_microbiological_working_areas [accessed Feb 19, 2016].



Types of compound

Alcohols

▶ 2. alcohols as preservatives:

- Benzyl alcohol
- Chlorobutol: decompose at acid pH during autoclaving
- Phenoxyethanol
- Bronopol: when exposed to light at alkaline pH → solutions decompose turning yellow or brown (decompose to formaldehyde and nitrite ions). Nitrite ion may react with amines to form nitrosamines (carcinogenic) *نیتروسامین*

Types of compound:

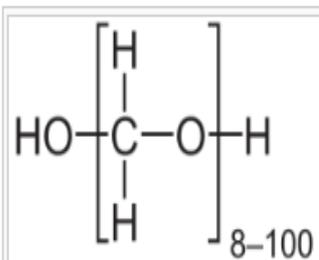
Aldehydes

I. Formaldehyde:

- ▶ **HCHO**
 - ▶ Can be used in either the **liquid or gaseous state** for disinfection
 - ▶ **Gaseous state** for disinfection of **isolators, safety cabinet, and rooms**
 - ▶ **Vapor is highly toxic and potentially carcinogenic if inhaled**
 - ▶ The **agent is not supplied as a gas** but either as **a solid polymer (paraformaldehyde)** or a **liquid (formalin)** which is **34-38% aqueous solution**
-
- ▶

Forms of formaldehyde [edit]

Formaldehyde is more complicated than many simple carbon compounds in that it adopts several different forms. As a gas, formaldehyde is colorless and has a characteristic pungent, irritating odor. Upon condensation, the gas converts to various other forms of formaldehyde (with different chemical formulas) that are of more practical value. One important derivative is the cyclic [trimer](#) metaformaldehyde or [1,3,5-trioxane](#) with the formula $(\text{CH}_2\text{O})_3$. There is also a linear polymer called [paraformaldehyde](#). These compounds have similar chemical properties and are often used interchangeably.



[Paraformaldehyde](#) is a common form of formaldehyde for industrial applications.

When dissolved in water, formaldehyde also forms a hydrate, [methanediol](#), with the formula $\text{H}_2\text{C}(\text{OH})_2$. This compound also exists in equilibrium with various [oligomers](#) (short polymers), depending on the concentration and temperature. A saturated water solution, of about 40% formaldehyde by volume or 37% by mass, is called "100% formalin". A small amount of [stabilizer](#), such as [methanol](#), is usually added to suppress [oxidation](#) and [polymerization](#). A typical commercial grade formalin may contain 10–12% methanol in addition to various metallic impurities. Aqueous formaldehyde is also called 'formalin'.

Occurrence [edit]

Processes in the upper [atmosphere](#) contribute up to 90% of the total formaldehyde in the environment. Formaldehyde is an intermediate in the oxidation (or [combustion](#)) of [methane](#), as well as of other carbon compounds, e.g. in [forest fires](#), [automobile](#)

Types of compound: Aldehydes



I. Formaldehyde (cont.):

- ▶ The gas is liberated by heating or mixing the solid or liquid with potassium permanganate and water
- ▶ Too irritant for routine application to skin



Types of compound: Aldehydes

لخفض انخفاض التهيجية
↓

▶ 2. formaldehyde-releasing agents:

▶ Have been developed to reduce the irritancy associated with formaldehyde while maintaining activity

✎ ① Noxythiolin (N-hydroxy N-methylthiourea):

- Dry powder

- On aqueous reconstitution slowly release formaldehyde a

② Polynoxylin

③ Taurolidine



Types of compound:

Biguanides

- ▶ I. Chlorhexidine:
- ▶ Cationic
- ▶ Activity reduced by anionic compounds
- ▶ Widespread use as antiseptic



Types of compound:

Halogens

▶ 1. Chlorine:

▶ Gaseous chlorine

▶ Liquid chlorine: made by compressing and cooling gaseous chlorine
تبييض

▶ 2. Sodium hypochlorites (bleach):

▶ It is preferable to prepare use-dilutions (working solutions) of hypochlorite on daily basis

▶ Undiluted bleach stored at room temperature in a closed container has a shelf life of about 6 months

▶ Storage of stock or working solutions of bleach in open containers causes release of chlorine gas → weaken antimicrobial activity



Types of compound:

Halogens

- ▶ 3. organic chlorine (chloramine) compounds:
- ▶ Such as chloramine-T, dichloramine-T and halazone → may be used for disinfection of contaminated drinking-water



Types of compound:

Halogens

- ▶ 4. Iodine:
 - ▶ Has a wide spectrum of antimicrobial activity: gram – ve, gram + ve, bacterial spores, mycobacteria, fungi and viruses
 - ▶ Elemental iodine I₂ is the active agent → ذائبيته ضعيفه بالمي
مشان صلابه ضر (iodophor)
 - ▶ 5. iodophors
 - ▶ Iodo (iodine) and phor (carrier)
 - ▶ An **iodophor** is a preparation containing iodine complexed with a solubilizing agent, such as a surfactant or povidone (forming povidone-iodine). The result is a water-soluble material that releases free iodine when in solution
 - ▶ Polyvinylpyrrolidone iodophors (PVP-I or povidine-iodine)
-





Types of compound:

Heavy metals

- ▶ Mercury and silver → استنداره مهم فلزات
- ▶ Largely replaced by less toxic compounds
- ▶ I. mercurials:
- ▶ Thiomersal, PMN, PMA → preservatives
- ▶ Use declines due to toxicity, hypersensitivity and local irritation



Types of compound:

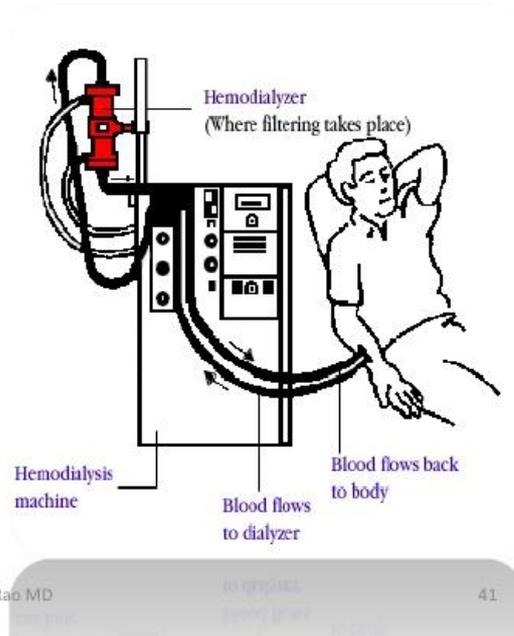
hydrogen peroxide and peracetic acid

- منصوب وفعال
لعمل
- ▶ High level disinfectants because of their production of highly reactive hydroxyl radical
 - ▶ Hydrogen peroxide works by producing destructive hydroxyl free radicals that can attack membrane lipids, DNA, and other essential cell components
 - ▶ Hydrogen peroxide is active against a wide range of microorganisms, including bacteria, yeasts, fungi, viruses, and spores
 - ▶ Combination of hydrogen peroxide and peracetic acid is synergistic → cold sterilant for dialysis machine
-



Per acetic acid and hydrogen peroxide useful in Hem dialyzers

- Findings demonstrated that this product inactivated all microorganisms with the exception of bacterial spores within 20 minutes. The combination of per acetic acid and hydrogen peroxide has been used for disinfecting hem



Cold Sterilants

The Renal Systems Group carries two types of cold sterilants. Renalin® 100 is used for reprocessing dialyzers with the Renatron® II 100 Series machine. Actril® is used for surface disinfection. Both products are a mixture of peracetic acid, hydrogen peroxide and acetic acid. They leave no toxic residues and after reacting with organic material, they decompose into oxygen and acetic acid. These cold sterilants destroy viruses, bacteria, spores and fungi.



Renalin® 100 Cold Sterilant



**Renalin® 100 Cold Sterilant
(For International Use Only)**



Actril® Cold Sterilant

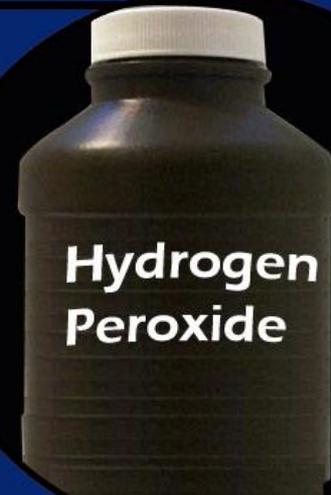




MotivateMe.in

تنظيف العدسات اللاصقة

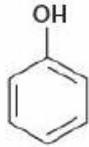
4) Cleanser for contact lens
Hydrogen peroxide disinfectant capacity is put to use in the contact lens cleaning solution. It is known that proteins get build up on lenses and using this chemical compound breaks the proteins.



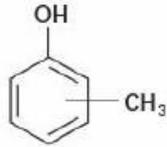
Types of compound:

Phenols

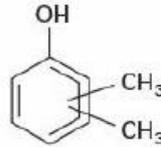
- ▶ Phenols naturally obtained by distillation of coal or petroleum (phenols, cresol, xylenols)
- ▶ Synthetic phenols: chlorocresol (p-chloro-m-cresol) and chloroxylenol (p-chloro-m-xyleneol)
- ▶ Chlorocresol → antiseptic & preservative
- ▶ Chloroxylenol → antiseptic & disinfectant
- ▶ Triclosan: two phenolic groups. Medicated soap, lotions, and solutions



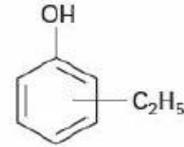
phenol
(A)



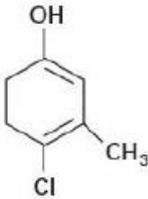
cresols
(B)



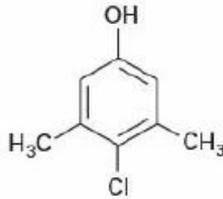
xylenols
(C)



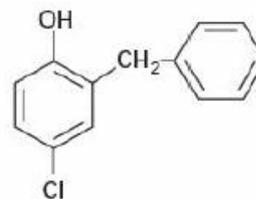
ethylphenols
(D)



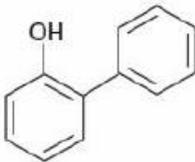
chlorocresol
(E)



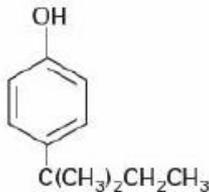
chloroxylenol
(F)



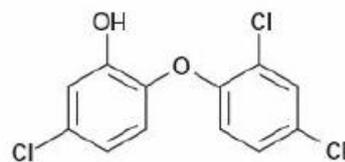
2-benzyl-4-chlorophenol
(G)



2-phenylphenol
(H)

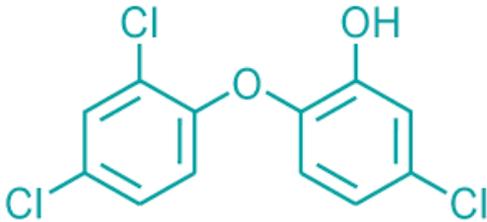


p-tert-amylphenol
(I)



triclosan
(J)

Structures of some common phenols possessing antimicrobial activity



Triclosan



Drug Facts	
Active ingredient	Purpose
Triclosan 0.46%.....	Antibacterial
Use For handwashing to decrease bacteria on the skin.	



Drug Facts	
Active ingredients	Purpose
Sodium fluoride 0.24% (0.14% w/v fluoride ion).....	Anticavity
Triclosan 0.30%.....	Antigingivitis
Uses aids in the prevention of: - cavities - plaque - gingivitis	
Warnings Keep out of the reach of children under 6 years of age. If more than used for brushing is accidentally swallowed, get medical help or contact a Poison Control Center right away. Ask a dentist before use if you have - bleeding or redness lasting more than 2 weeks - pain, swelling, pus, loose teeth, or more spacing between teeth These may be signs of periodontitis, a serious form of gum disease.	

Helps Prevent: Cavities - Gingivitis - Plaque | Fights Tartar - Freshens

Colgate
Anticavity Fluoride and Antigingivitis Toothpaste
NET WT 6.0 OZ (170 g)

Questions

- ▶ What is the active ingredient in Dettol?
- ▶ Why it produces a white emulsion when diluted with water ?
- ▶ Why pine oil is added?

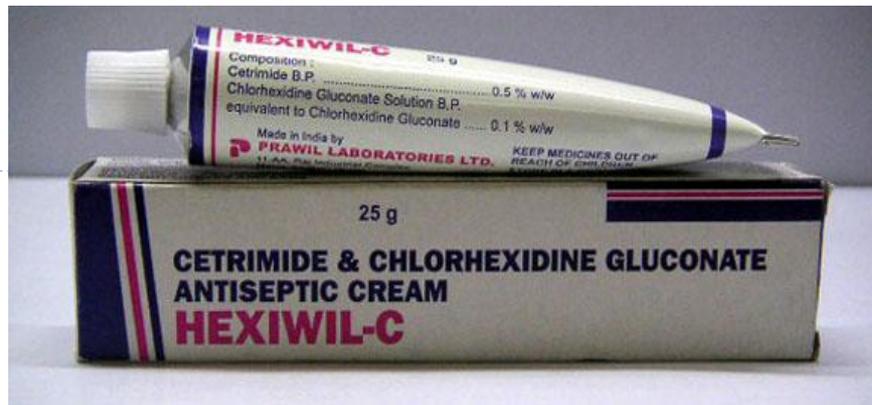


Types of compound:

Surface-active agents

- ▶ Anionic and non-ionic surface active agents have strong detergent properties but exhibit little or no antimicrobial activity
 - ▶ Ampholytic or amphoteric display both detergent properties of the anionic surfactant and the antimicrobial activity of the cationic agents → hand scrubbing, medical instrument and floor disinfection in hospitals
 - ▶ Cationic surfactant (quaternary ammonium compounds) → most important role in antimicrobial:
 - Benzalkonium chloride
 - Cetyltrimethylammonium bromide (cetrimide)
-





meijer kids!

Paraben Free

Bright Colored Foam

antibacterial foaming hand soap

Cherry

10.1 FL OZ (298 mL)

meijer kids!

This colored foaming hand soap makes washing your child's hands more fun! Our special antibacterial formula is designed to help kill germs, keeping your child's hands clean, and smelling delicious!

Drug Facts	
Active ingredient	Purpose
Benzalkonium Chloride 0.20%	Antiseptic
Use • hand washing to decrease bacteria on skin.	
Warnings For external use only.	
When using this product avoid contact with eyes, if contact occurs, rinse thoroughly with water.	
Discontinue use if irritation and redness develop.	
Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away.	
Directions • wet hands • work into rich lather • rinse well	
Inactive ingredients Benzalkonium Chloride, Benzophenone-4, Citric Acid, Cocamidopropyl Betaine, Fragrance (Parfum), Methylisothiazolone, Phenoxyethanol, Red 33, Red 40, Sodium Lauryl Sulfate, Sodium Lauryl Sarcosinate, Tocopheryl Acetate, Water (Aqua).	
Questions? 1-800-FDA-1088	

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Antimicrobial combinations

- ▶ All chemical agents have their limitations (antimicrobial activity, resistance to organic matter, stability, incompatibility, irritancy, toxicity, or corrosivity)
- ▶ Combination:
 - Improve activity
 - Reduce toxicity
 - Synergistic



Table 19.7 Disinfection policies—classification of equipment according to risk

Risk level	Examples	Classification	Objective	Decontamination
High risk: critical items	Surgical instruments, implants, catheters	Objects which enter a sterile tissue or system	Sterility—all microorganisms killed including bacterial spores	Thermal or gaseous sterilization preferable. Chemical sterilization with aldehyde or peroxygen with extensive contact times
Intermediate risk: semicritical items	Endoscopes, cystoscopes, respiratory and anaesthesia equipment	Objects in contact with mucous membranes or broken skin	Free of all viable microorganisms except bacterial spores	High level disinfection with aldehyde or peroxygen; contact times up to 30 min
Low risk: non-critical items	Blood pressure cuffs, food utensils, furniture, floors	Objects in contact with intact skin but not mucous membranes	Some microorganisms remaining	Low-level disinfection using alcohols, chlorine, iodophor, QACs

QAC, quaternary ammonium compound.

Table 19.3 Antifungal activity of disinfectants and antiseptics

Antimicrobial agent	Time (min) to give >99.99% kill ^a of		
	<i>Aspergillus niger</i>	<i>Trichophyton mentagrophytes</i>	<i>Candida albicans</i>
Phenolic (0.36%)	<2	<2	<2
Chlorhexidine gluconate (0.02%, alcoholic)	<2	<2	<2
Iodine (1%, alcoholic)	<2	<2	<2
Povidone-iodine (10%, alcoholic and aqueous)	10	<2	<2
Hypochlorite (0.2%)	10	<2	5
Cetrimide (1%)	<2	20	<2
Chlorhexidine gluconate (0.05%) + cetrimide (0.5%)	20	>20	>2
Chlorhexidine gluconate (0.5%, aqueous)	20	>20	>2

^aInitial viable counts $c.1 \times 10^8$ /ml in suspension test.

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