



Anti-Infective Agents

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History of Chemotherapy

- Latter half of 19th century
- Paul Ehrlich: Ehrlich's principles of chemotherapy (1904):
 - ✓ chemicals could directly interfere with the proliferation of microorganisms (MOs)
 - ✓ at concentrations tolerated with the host.
- This concept is popularly known as the magic bullet:
 - ✓ could search out & destroy invading microorganism
 - ✓ without adversely affecting the host
- Selective toxicity: greater toxicity to microorganisms
- Chemotherapeutic index: therapeutic index: compare Min. effective dose to Max. tolerable dose

Anti-Infective Agents & Meaning of Related Keywords

- **Local** acting known as:
 - ✓ **germicide**: prevent infection by inhibiting growth or action of MO
 - ✓ **sanitizer**: reduce microbial load from an inanimate surface
 - ✓ **antiseptic**: disinfecting chemical agent:
agent used to inhibit bacterial growth *in vitro* & *in vivo*
 - ✓ **disinfectant**: agent to **kill** MO in inanimate environment
 - ✓ **detergent**: a surfactant with cleaning efficacy on surfaces
 - ✓ **sterilant**
- hand hygiene
- **Biologically** systemic acting anti-infective agents as:
 - ✓ preservative
 - ✓ anti-protozoal; anti-parasitic; anti-bacterial; anti-fungal;
 - ✓ anti-tubercular (anti-mycobacterium); anti-malarial;
anthelmintic

TABLE 50–2 Commonly used terms related to chemical and physical killing of microorganisms.

Antisepsis	Application of an agent to living tissue for the purpose of preventing infection
Decontamination	Process that produces marked reduction in number or activity of microorganisms
Disinfection	Chemical or physical treatment that destroys most vegetative microbes and viruses, but not spores, in or on inanimate surfaces
Sanitization	Reduction of microbial load on an inanimate surface to a level considered acceptable for public health purposes
Sterilization	A process intended to kill or remove all types of microorganisms, including spores, and usually including viruses, with an acceptably low probability of their survival
Pasteurization	A process that kills nonsporulating microorganisms by hot water or steam at 65–100°C

Factors Involved in Effectiveness of Anti-Infective Agents

- MO intrinsic resistance
- Number of MO
- Target size
- Duration exposure time
- Temperature of exposure
- pH of target environment
- Hydration of target environment

Chemical Classification of Local Anti-Infective Agents

- **Alcohols:** EtOH; isopropyl alcohol
- **Acids:** acetic acid; benzoic acid; p-OH-benzoic acid
- **Iodine:** alcoholic solution; povidone iodine
- **Aldehydes:** formalin (formaldehyde); Glutaraldehyde
- **Phenols:** alkyl; aryl; para-halogen: Phenol Coefficient
- **Oxidizing agents:** peroxides
- **Halogen containing derivatives**
- **Cationic surfactants & structures:** aryl alkyl ammonium; biguanides
- **Mercurial salts & derivatives**
- **Polycyclic aromatics:** dyes
- **Ethylene oxide:** as sterilant
- **Nitrofurans derivatives**
- **Miscellaneous**

Activity Potential of Antiseptic Agents

TABLE 50–1 Activities of disinfectants.

	Bacteria				Viruses		Other		
	Gram-Positive	Gram-Negative	Acid-Fast	Spores	Lipophilic	Hydrophilic	Fungi	Amebic Cysts	Prions
Alcohols (isopropanol, ethanol)	HS	HS	S	R	S	V	—	—	R
Aldehydes (glutaraldehyde, formaldehyde)	HS	HS	MS	S (slow)	S	MS	S	—	R
Chlorhexidine gluconate	HS	MS	R	R	V	R	—	—	R
Sodium hypochlorite, chlorine dioxide	HS	HS	MS	S (pH 7.6)	S	S (at high conc)	MS	S	MS (at high conc)
Hexachlorophene	S (slow)	R	R	R	R	R	R	R	R
Povidone, iodine	HS	HS	S	S (at high conc)	S	R	S	S	R
Phenols, quaternary ammonium compounds	HS	HS	MS	R	S	R	S	—	R

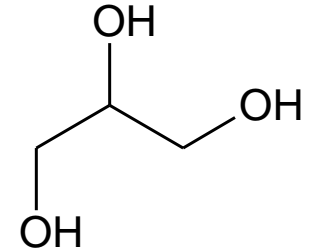
conc, concentration; HS, highly susceptible; MS, moderately susceptible; —, no data; R, resistant; S, susceptible; V, variable.

Alcohols as Anti-Infective Agent

- Ethanol: $\text{CH}_3\text{CH}_2\text{OH}$
- Isopropyl alcohol: $(\text{CH}_3)_2\text{CHOH}$
- 60-90% by volume in water: efficient partition coefficient
- MOA: protein denaturation
- Alcohol based hand rubs is suggested by CDC(P)
- Consider **inflammability** of alcohol
- Rapidly active against vegetative MO including bacteria even MT, fungi & inactivating lipophilic virus
- **Not** against spores & hydrophilic viruses

Alcohol & Iodine Mixture as Anti-Infective Agent

- Glycerin Iodide:
 - ✓ iodine (0.15-15%) & glycerin (30-87%)
 - ✓ iodinated glycerol
 - ✓ a homogenous solution

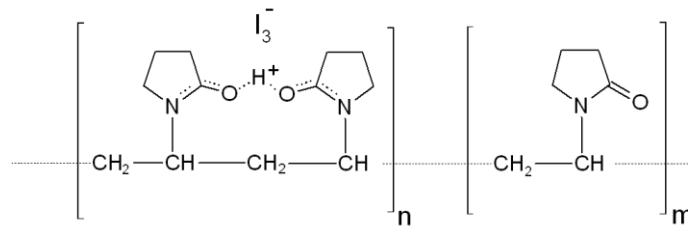


Iodine Tincture as Anti-Infective Agent

- I_2 in 1:20,000 dilution in alcohol: bactericidal
- I_2 (2%) & NaI (2.4%) in alcohol
- Disadvantage: sensitivity & staining characteristics

Iodine (Povidone Iodine: Betadine®) as Anti-Infective Agent

- Povidone: Poly-Vinyl Pyrrolidone (PVP)
- A iodophore: provides I₂ in 1:20,000 or 0.005% dilution: bactericidal
- MOA: protein denaturation & bacteria precipitation
- Against virus, bacteria, spore, fungi & protozoa
- Sporicidal but **not** persistent activity
- Sore throat gargle: 1% w/v PVP-I₂; 0.1% w/v I₂



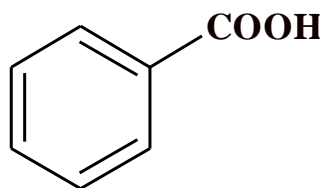
Sara RAmini, Nov2024



Acids as Anti-Infective Agent

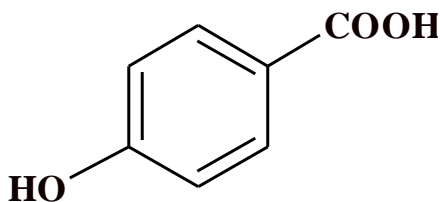
- Acetic acid: CH_3COOH

- Benzoic acid:



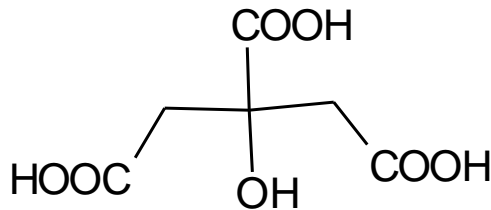
- ✓ as preservative

- p-OH-benzoic acid

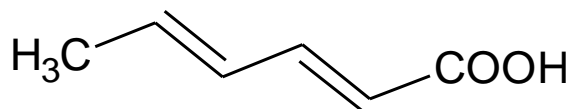


- ✓ as preservative

- Citric acid

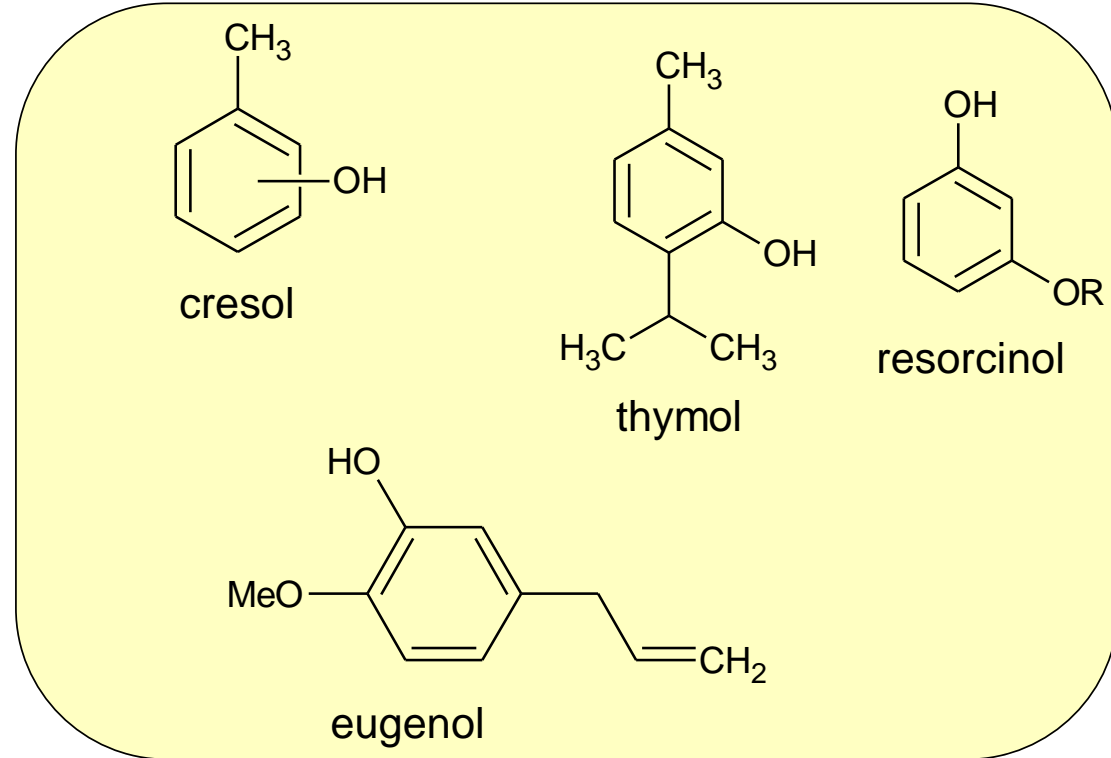


- Sorbic acid



Phenols as Anti-Infective Agent

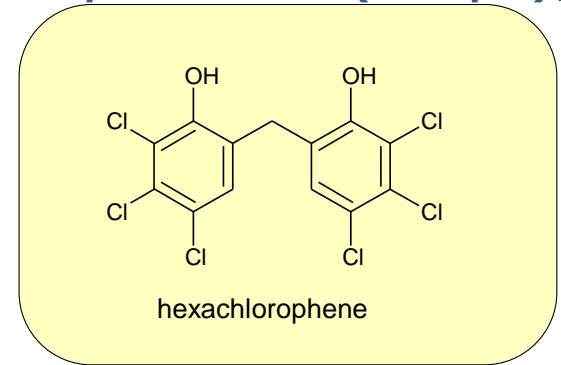
- Phenol derivatives:
 - ✓ cresol: alkylated phenol
 - ✓ thymol: alkylated phenol
 - ✓ resorcinol
 - ✓ eugenol
- MOA:
 - ✓ disrupt CW & CM of MO
 - ✓ precipitate proteins
 - ✓ inactivates enzymes
 - ✓ proteolytic: 5-7%
- Consider phenol coefficient



Phenols as Anti-Infective Agent: Hexachlorophene

- Organo-chlorine compound
- ✓ 2-3% solution in surgical scrub, handwash products (soaps), toothpaste & detergent creams

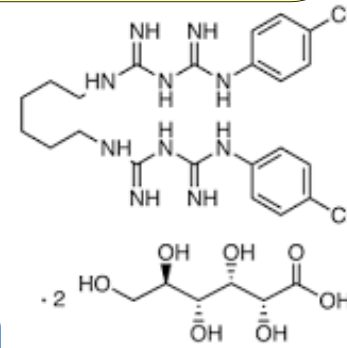
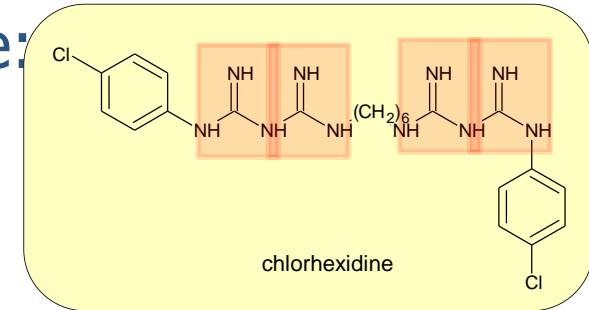
- MOA: bacteriostatic



- SE: CNS toxicity; skin damage in long exposure:
- ✓ hence, was banned as non-prescription agents since 1972

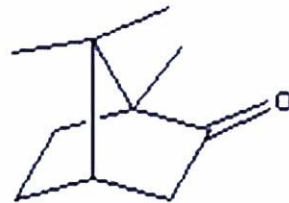
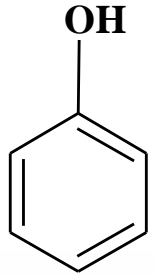
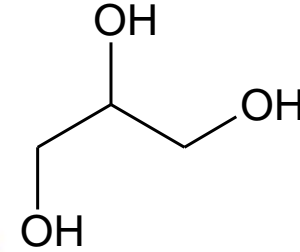
Biguanide as Anti-Infective Agent: Chlorhexidine

- Chemistry: bi-guanide like cationic structure:
 - ✓ di-cation form in physiological pH
 - ✓ with **no** systemic absorption
- Low water solubility:
 - ✓ improved water solubility in di-gluconate salt
- **MOA**: strongly adsorbed on MO cell membrane:
 - ✓ cause leaking membrane
 - ✓ active in pH=5.5 to 7; 4% is optimum concentration
- In combination with alcohol: rapid, retained & persistent activity
- Topical & local antiseptic applied in:
 - ✓ pre-operative skin disinfection; wound irrigation
 - ✓ mouthwash: as **prescription** item: in gingivitis & gum inflammation
- **In**activated with anionic detergents

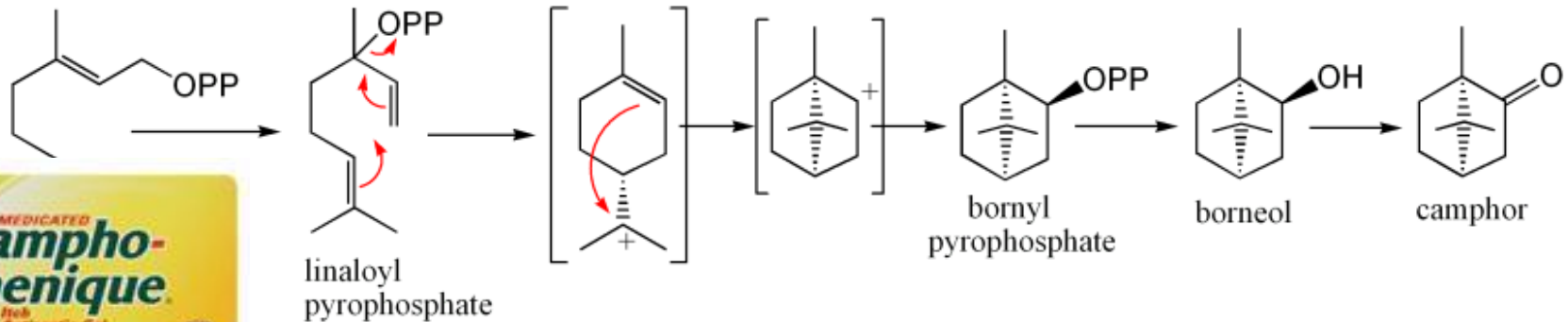


Alcohol/Phenol as Anti-Infective Agent

- Glycerin Phenique or Phenol Glycerin:
 - ✓ prepared of : glycerin & phenol:
 - ✓ +/- camphor
- applied as ear drop



CAMPHOR

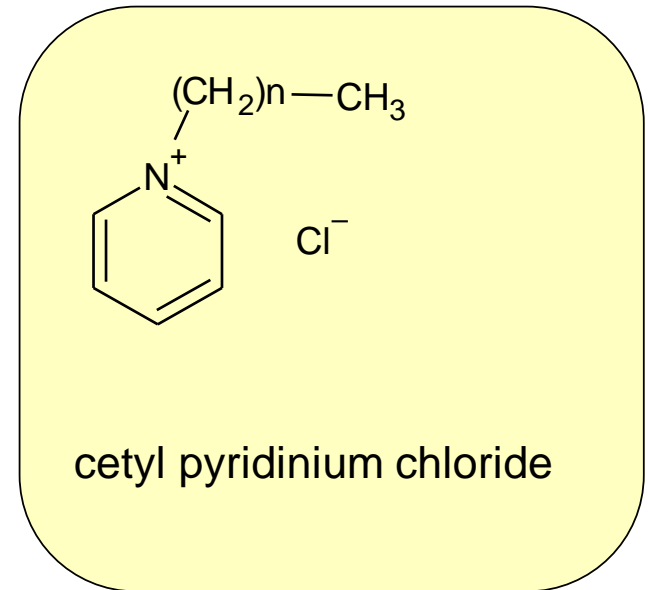


Halogen Containing Derivatives as Anti-Infective Agents

- Inorganic chlorine derivatives: sodium hypochlorite (5.25%)
- N- chloro derivatives:
 - ✓ to produce HClO (hypochlorous acid) in aqueous media
- 5 to 10000 ppm regarding the type of MO
- ClO⁻: less active than HClO
- MOA:
 - ✓ oxidation of thiol (-SH) in proteins
 - ✓ N- chlorination of amino acids

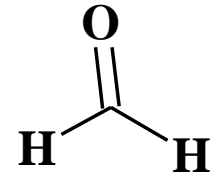
Cationic Surfactants as Anti-Infective Agents

- Cetyl pyridinium Chloride:
 - ✓ chemistry: alkyl pyridinium derivatives
- Applied in:
 - ✓ mouth wash
 - ✓ throat lozenges

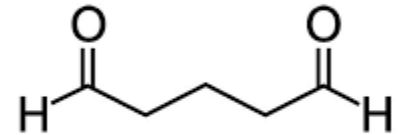


Aldehydes as Anti-Infective Agents

- Formalin (formaldehyde: HCHO): 4 to 40%



- Glutarol (glutaraldehyde): 2-10%



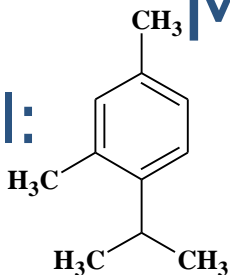
- pH is important in the efficacy
- Against wart

Mouthwash: Listerine®

LISTERINE® TOTAL CARE



Menthol:



Eucalyptol or cineol:

✓ monoterpenoid bicyclic ether

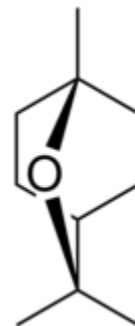
✓ cooling taste

✓ insoluble in water; camphor like odor

• Insecticidal & insect repellent

✓ Relieves throat irritation

✓ Weak κ opioid receptor agonist



Active Ingredients

Eucalyptol 0.091% w/v, Thymol 0.063% w/v, Menthol 0.05% w/v, Sodium Fluoride 0.05% w/v, Zinc Chloride 0.09 % w/v

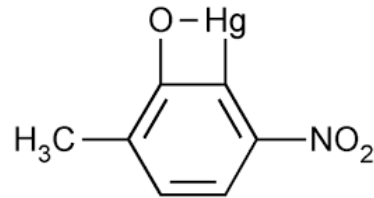
Inactive Ingredients

Alcohol, Aroma (flavor), Benzoic Acid, Blue 1, Methyl Salicylate, Poloxamer 407, Red 40, Sodium Benzoate, Sodium Saccharin, Sorbitol, Sucralose, Water (eau)

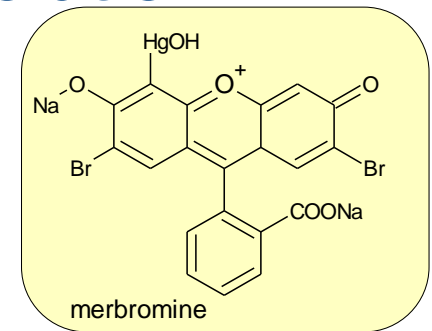
Mercural Derivatives as Anti-Infective Agents

- Ammonium mercury chloride: salts of Hg: $\text{Hg}(\text{NH}_2)\text{Cl}$

- ✓ Nitromersal



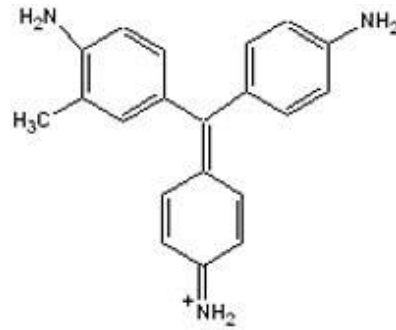
- ✓ merbromine (mercuro-chrome): 2% solution:



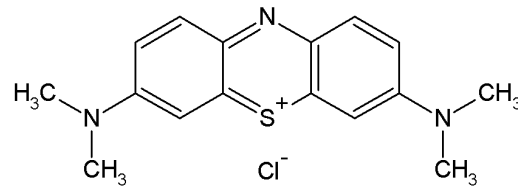
- Clinical effect: antiseptic: bacteriostatic

Polycyclic Aromatic Dyes as Anti-Infective Agents

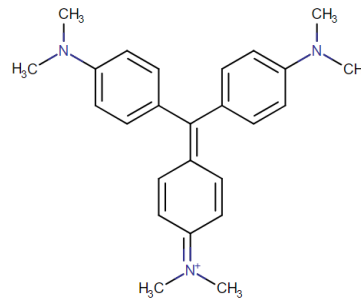
• Basic fuschine



• Methylene blue



• Gentian violet: hexa-methyl p-rosaniline



• MOA: interacts positive ions in CW & DNA