# Advancing wound care: Antiseptic strategies – povidone-iodine

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## Abstract

Microbial contamination remains a major challenge in wound healing and is frequently associated with delayed tissue repair, chronic infection and additional tissue damage. Effective management of microbial burden is, therefore, a central objective in wound care. In this context, topical antiseptics play an important role in limiting microbial proliferation and supporting the healing process.

This review examines the pharmacological properties of commonly used antiseptics in wound management. Particular attention is given to their mechanism of action, antimicrobial spectrum of activity and potential for resistance development. The antiseptics discussed include iodine-based products, biguanides such as chlorhexidine, octenidine, oxidising agents, silver-containing formulations and honey as a natural therapeutic agent.

Unlike antibiotics, which typically act on specific molecular targets, antiseptics exert their broad-spectrum antimicrobial activity through multiple mechanisms. These include disruption of microbial cell membranes, protein denaturation and oxidative damage. Because several cellular targets are affected simultaneously, the likelihood of rapid resistance development is generally reduced.

The selection of an appropriate antiseptic should not rely solely on antimicrobial potency. Factors such as cytotoxicity, tissue compatibility and overall safety must also be considered. Careful selection of antiseptic agents, guided by current evidence, is therefore essential to optimise wound-healing outcomes, while supporting responsible stewardship in pharmacy practice.

**Keywords**: antiseptics, iodine, chlorhexidine, wound healing, antimicrobial resistance

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## Introduction

Topical antibiotics have been considered the treatment of choice for skin infections and infected wounds for many years. However, with the emergence of antimicrobial resistance, the topical use of antiseptics has experienced a renaissance in recent years.[1,2] Concerns about the apparent cytotoxicity of traditional antiseptics led clinicians to be reluctant to use them in wound management.[3]

The normal wound-healing process involves a tightly regulated sequence of inflammation, proliferation and remodelling, mediated by fibroblasts, keratinocytes, endothelial cells and macrophages.[2] However, when a wound fails to progress through the phases of wound healing, chronic wounds may occur. Therefore, a wound infection is defined as the "invasion of a wound by proliferating microorganism to a level that invokes a local and/or systemic response in the host", according to the International Wound Infection Institute.[4]

## Comparative analysis: antiseptics, disinfectants and antibiotics

Clear differentiation between antiseptics, disinfectants and antibiotics is essential for appropriate therapeutic selection. The term *antiseptic* is derived from the Greek word *anti* (against) and *sepsis* (rot); literally meaning "against rot".[5] Historically associated with infection prevention, antiseptics are now defined pharmacologically as chemical agents used on skin and mucous membranes to inhibit or destroy microorganisms. Importantly, antiseptics generally exhibit broad-spectrum activity, enabling them to target multiple types of microorganisms simultaneously.[5]

Disinfectants eliminate microorganisms in their active state and inhibit microbial reproduction but are intended for use on inanimate surfaces due to potential tissue toxicity. While topical antibiotics are commonly formulated as creams and ointments, they do not facilitate autolytic debridement or help regulate the moisture management within the wound bed.[5] Another important distinction concerns antimicrobial resistance. Resistance to antibiotics may arise from a single mutation, whereas resistance to topical antiseptics often requires multiple mutations.[6] Antiseptics are typically broad-spectrum and may demonstrate antibacterial, antifungal, and antiviral activity. This broader mechanism of action and lower propensity to develop single-step resistance underscore the relevance of antiseptics in contemporary wound care practice.[5] Early and appropriate application is therefore considered an important component of infection prevention strategies in wound care.[7,8]

## Classification and pharmacological action

Several antiseptic classes are commonly employed in wound care practice. Antiseptics exert their effects through pharmacological, metabolic and/or immunological mechanisms. Antiseptics are generally classified as halogenated compounds, alcohol-based agents, biguanides, and quaternary ammoniums. Each class differs in modes of action, antimicrobial spectrum, cytotoxicity profile, tissue compatibility, and suitability for acute versus chronic wounds, as summarised in Table I.

**Table I:** Antiseptics classification, examples and application[4-10]

| Classification | Mode of action | Examples | Application |
|---|---|---|---|
| **Halogenated oxidising compounds** | | | |
| Chlorous agents | Superoxide radicals damage enzymes in the cells and promote apoptosis cell death | Sodium hypochlorite (NaOCl)<br>Hypochlorous acid (HOCl)<br>Dakin's solution (0.05%) | • Act as surface surfactant (0.0125–0.05%)<br>• Antiseptic for skin and mucosal wounds (0.005–0.01%)<br>• Surgical site antiseptic (0.01–0.05%)<br>• Irrigate traumatic, acute or chronic wounds without drainage, e.g., peritoneal cavity<br>• Requires accurate pH monitoring, temperature control, and proper storage (pH above 11 at 20 °C)<br>• No absorption in intact cell layer<br>• Allergic reaction and dermatitis may be observed<br>• Fair biofilm activity<br>• Excellent tissue compatibility<br>• Effectiveness depends on protein load and wound exudate |
| Iodine-based agents | Releases free iodine from a neutral polymer base, causing oxidation and iodination of fatty acids, amino acids and nucleic acids leading to cell membrane destabilisation | Povidone-iodine (PVP-I) | • Intraoperative rinse reduces incidence of infection (4% PVP-I)<br>• Dilutions of 0.1–1% work faster than a 10% solution due to an increase of free iodine in the solution<br>• 1% solution is sporicidal against spores of *Bacillus subtilis* in 28–93 minutes for a 99% kill<br>• Broad spectrum of antimicrobial activity<br>• Inhibit biofilm development by *Staphylococcus epidermidis (S. epidermidis)*, *Staphylococcus aureus (S. aureus)*, *Klebsiella pneumoniae (K. pneumoniae)*, *Pseudomonas aeruginosa (P. aeruginosa)* and *Candida albicans* (*C. albicans*)<br>• Quick onset of action within 15 seconds–1 minute<br>• Suitable for sharp, cut and lacerated superficial skin and mucous membrane wounds<br>• Not recommended for chronic wounds due to its cytotoxicity<br>• Not teratogenic, neurotoxic or mutagenic<br>• PVP-I is not recommended in newborns, young children, pregnancy or lactation<br>• Contraindicated in thyroid disease and iodine radiotherapy<br>• PVP-I less irritating to the skin than ordinary iodine solution<br>• Risk for allergic reaction in iodine-sensitive individuals (low prevalence of 0.4%)<br>• Fair tissue compatibility<br>• Do not use long term |
| Alcohol-based compounds | Denaturation of microbial protein component | Ethanol (alcohol)<br>Isopropyl alcohol (isopropanol) | • Optimum concentration: 60–95 % in water: bactericidal, virucidal, mycobactericidal<br>• 70% concentration: skin disinfectant; instrument disinfectant<br>• 70%: preoperative skin disinfectant<br>• Effective combination with chlorhexidine and iodine<br>• Isopropyl alcohol: greater bactericidal than ethanol but twice as toxic |
| Biguanides | Negatively charged phosphate phospholipid groups bind to the bacterial cell wall, disrupting membrane function and microbial cell death | Polyhexamethylenebiguanide (PHMB) | • Colourless, odourless, non-corrosive, water- and alcohol soluble<br>• Bactericidal within 15–30 minutes<br>• Low absorption to epidermis<br>• Commercially prepared in combination with betaine or Ringer's solution<br>• Concentrations of 0.02%, 0.04% and 0.1%. are sufficient<br>• Impregnated dressings completely eliminate *S. epidermis* strains within 24 hours<br>• Effective against Gram-positive, Gram-negative bacteria and *C. albicans*<br>• Large margin of safety.<br>• Good–excellent tissue compatibility<br>• Excellent tissue compatibility |
| | | Chlorhexidine | • Safe dilutions 0.05–2% solution or gels<br>• Wound irrigation and cleaning<br>• Use as preoperative skin antisepsis and not for wound treatment<br>• Prophylaxis against superficial surgical site infection (SSI), bloodstream infection<br>• Fair biofilm activity<br>• Poor tissue penetration<br>• Undiluted solutions are cytotoxic and delay wound healing<br>• Not to be used on chronic wounds |

**Table I:** *Continued*

| Classification | Mode of action | Examples | Application |
|---|---|---|---|
| Quaternary ammoniums | Cationic, surface-active compound allowing OCT to bind to negatively charged surfaces enveloping microbial cell membranes, causing structural disruption | Octenidine (OCT) | • Handwashing gels (0.05–1%)<br>• 0.05–1% concentration microbicidal in 1 minute against bacteria and fungi (*S. aureus*, *C. albicans*)<br>• Acute, traumatic and infected wounds at 0.1% concentration in combination with phenoxyethanol<br>• Oral cavity disinfectant<br>• OCT gels are suitable for burn wounds; superior to PVP-I and silver-containing products<br>• Not absorbed through the skin<br>• Safe to use in babies, pregnant and breastfeeding women<br>• OCT-coated tracheostomy tubes reduce infection in ventilated patients<br>• Coat surgical sutures<br>• Good biofilm activity<br>• Excellent tissue compatibility<br>• Suitable for chronic wounds |
| Nanocrystalline silver | Impairs cell membrane permeability by modifying bacterial membrane proteins, reacts with sulphur and phosphorus in membrane DNA, leading to $H^+$ leakage and cell death (apoptosis) | | • Used as gel and impregnated dressings<br>• Medical devices coating<br>• Nanoparticle size and shape determine biochemical, physical and antimicrobial properties<br>• Smaller than 10 nm and triangular shape is best<br>• Poor biofilm activity<br>• Fair tissue compatibility<br>• Bactericidal activity against Gram-negative and Gram-positive bacteria, fungi and viruses<br>• Resistant organisms: *E. coli*, *P. aeruginosa*, *K. pneumoniae* |
| Honey | Immunomodulatory activity<br>Polyphenols in honey accelerate hydroxyl radical formation ( $H_2O_2$) and oxidative strand breakage of DNA | | • Pure honey, gel or dressings<br>• Fair biofilm activity<br>• Excellent tissue compatibility<br>• Appropriate for most wounds<br>• Used in conjunction with other antimicrobial agents<br>• Effective against several Gram-positive and Gram-negative skin pathogens (*E. coli*, *S. aureus*) |

## Therapeutic index

According to Geng et al., higher therapeutic indices (TIs) indicate better safety and effectiveness.[6] The therapeutic indices for the topical antiseptics were predominantly low, typically ranging from 0.5–3.0. Hypochlorous acid produced the highest therapeutic index (TI) for *P. aeruginosa* (8.81), *S. aureus* (6.31) and *E. coli* (5.49). The highest TI value for methicillin-resistant *S. aureus* (12.1) was observed with polyhexamethylene biguanide. The TI of a topical antiseptic was calculated as the ratio of the mean cytotoxic concentration (CT50) in a mammalian cell line to the mean bactericidal concentration (MBC) of a bacterial species. A low value indicates low effectiveness, while higher values indicate high effusiveness ratios.[6]

## Ideal antiseptic product

Antiseptics should be safe for general use, free of causing allergic reactions or pain, and not toxic, carcinogenic, or mutagenic. Furthermore, they must not impede the wound healing process. The ideal properties are summarised in Table II.

**Table II:** Properties of an ideal antiseptic product[4]

| Properties of an ideal antiseptic product |
|---|
| It is not toxic, carcinogenic or mutagenic |
| Non-traumatic |
| Does not cause an allergic reaction |
| Does not cause pain |
| Can handle excess wound exudate |
| It is fast-acting in acute wounds |
| Does not cause resistance or cross-resistance |
| Ability to penetrate biofilm |
| Suitable chemical and physiological properties that do not colour the skin, an acceptable smell and a suitable consistency |
| Cost-effective |
| Easy and safe to use |
| Tolerability equal to physiological saline |

## Comparative clinical efficacy: povidone-iodine

Recent clinical evidence underscores the therapeutic value of povidone-iodine (PVP-I) across various wound care and surgical settings. A systematic review by Barringah-Benissan et al. found that iodine-based treatments were associated with significantly better wound-healing outcomes than saline irrigation, with a

relative risk (RR) of 1.85 (95% CI, 1.27–2.69).[7] The clinical utility of PVP-I is largely due to its broad antimicrobial spectrum. According to a narrative review by Alves et al., the extensive antimicrobial spectrum of PVP-I is more beneficial than the restricted antimicrobial activity exhibited by polyhexanide (PHMB) and silver-containing products.[2]

Furthermore, the role of PVP-I in surgical prophylaxis remains robust. In a large-scale randomised controlled trial involving 3360 patients, PVP-I in alcohol was found to be noninferior to chlorhexidine gluconate in alcohol for preventing surgical site infections (SSIs) following cardiac or abdominal surgery.[11]

## Conclusion

In summary, the management of the wound microenvironment remains a complex clinical challenge, necessitating a transition from passive cleaning toward proactive, evidence-based antisepsis. While the introduction of newer agents such as polyhexanide and silver-based products has expanded the clinical toolkit, established halogenated compounds, especially PVP-I, continue to demonstrate robust efficacy and a broad antimicrobial spectrum, remaining noninferior to more modern alternatives in many settings. The selection of a topical antiseptic must be guided by the TI, balancing potent bactericidal activity with preservation of mammalian cell viability. As the clinical threat of single-step antibiotic resistance continues to grow, the multi-target mechanisms of broad-spectrum antiseptics offer a sustainable and effective strategy for mitigating microbial burden, preventing early biofilm formation and facilitating the physiological progression of wound healing.

### *Conflict of interest*

The author declares no conflict of interest.

### *Ethical approval*

Ethical approval was not required.

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