

REVIEW



Povidone Iodine -Revisited

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ABSTRACT:

Povidone Iodine or polyvinyl pyrrolidone-iodine is an iodophor and a broad spectrum antimicrobial agent delivered in many forms including powders, gels, lotions, ointments, sprays and mousses. Compared to other similar compounds Povidone iodine is highly soluble and less toxic making it widely suitable for surgical asepsis and wound dressing. In dentistry it is used for pre surgical skin preparation, pre procedural rinse to reduce bacteremia and microbial load in aerosols, root canal irrigant and intracanal medicament.

Key words: Povidone Iodine, Iodophor, Asepsis, Disinfection

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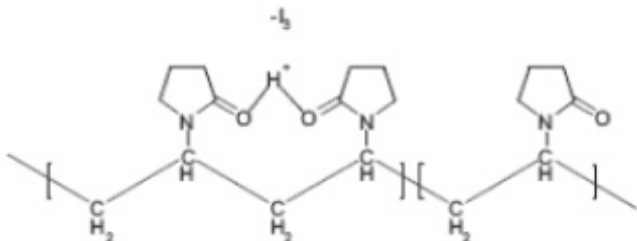
Introduction:

Povidone Iodine or polyvinyl pyrrolidone-iodine, commonly abbreviated as PVP-I was discovered by American scientists H. A. Shelanski and M. V. Shelanski. PVP-I was introduced to the pharmaceutical market as an antiseptic agent in the 1950's and is found to be more effective than other iodine formulations and was less toxic.

Structure:

PVP-I is 2-Pyrrolidinone, 1-ethenyl-, photopolymer, compound with iodine¹

CHEMICAL STRUCTURE



Properties:

PVP iodine is a loose complex of elemental iodine with a neutral, amphipathic organic

compound, poly vinyl pyrrolidone, which serves as a sustained release reservoir of iodine. PVP-I is a broad spectrum biocidal agent which is highly soluble than other iodine compounds like Tincture of iodine and Lugol's solution. PVP-Iodine is also soluble in: ethyl alcohol, isopropyl alcohol, glycols, glycerin, acetone and polyethylene glycol.² Povidone iodine is highly stable when stored away from moisture and light. PVP-I is effective in the range of pH 3 -6 and average particle size ranges from 90 to 140µ.

Bio-Compatibility:

PVP-I differs from iodine, in that it is less irritating to the skin and does not require iodides or alcohol to dissolve. Additionally, PVP-I stains are water-washable. Compared to other preparations, PVP-iodine exhibits markedly lower oral toxicity. Consequently, the accidental ingestion of PVP iodine solution is much less hazardous than from equal amounts of available iodine solutions. For this reason, PVP-iodine solutions do not require the hazardous, poisonous warning labels on bottles that iodine products must have. PVP-I is delivered in many forms including powders, gels, lotions, ointments, sprays and mousses. However the efficacy of action is dependent on available free iodine.

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Mode of Action:

In the PVP-Iodine complex, the iodine does not exist as a single species, and in fact several forms of iodine have been characterized:

- **Available iodine:** Contains all the iodine species which can be titrated with sodium thiosulfate
- **Iodide:** Negatively charged ion; necessary for the complexation of iodine
- **Total iodine:** Given by the sum of available iodine and iodide.
- **Free iodine:** The type of iodine which can be extracted from aqueous PVP-Iodine solution.

The disinfecting characteristics of iodine arise from its ability to substitute for covalently bound hydrogens in compounds containing -OH, -NH, -SH, or CH functional groups. PVP-I being a polymeric iodophor, reacts with oxygen containing functional groups. The difference between a conventional iodine solution and an iodophor is that the latter carries practically all the iodine in a complexed form, so that the concentration of the free iodine in the solution is always very low. This property has the effect of reducing the drawbacks associated with the presence of elemental iodine i.e. high toxicity, high level of irritation and staining power.³

Biocidal action:

PVP-Iodine is used in both human and veterinary medicine to kill on contact a wide variety of bacteria, viruses, fungi, protozoa and yeasts. The determining factor of the bactericidal action of PVP-I remains the concentration of free iodine.³ In pharmaceutical formulations that contain both iodine and iodide, the bactericidal effect can almost entirely be attributed to free molecular iodine.³

The microbiocidal action of PVP-Iodine, as discussed earlier, is related to the non-complexed, freely mobile elemental iodine, I₂, the active form of which is polarized by water and hence can be considered to be H₂OI⁺ in its final state. This activated iodine reacts in electrophilic reactions with enzymes of the respiratory chain as well as with amino acids from the cell membrane proteins both located in the cell wall. As a result, the well-balanced tertiary structure necessary for maintaining the respiratory chain is destroyed and the microorganism irreversibly damaged. Consequently, PVP-Iodine has a nonspecific mode of action.

PVP-I at concentrations more than 0.5% has shown

to be rapidly virucidal. Studies have shown that PVP-I 0.25% surgical scrub and solution inactivated HIV within seconds in-vitro, and if used in clinically achievable concentrations could serve as a surface disinfectant in hospital settings where HIV may be present. PVP-I was the most effective when compared with benzalkonium chloride and chlorhexidine digluconate, since it also yielded negative results in the HIV-specific plaque forming assay.⁴

Table: 1 Efficacy of PVP-I against different micro-organisms⁵

Organisms	PVP-I (available iodine range in ppm)	Contact kill time in seconds
Staphylococcus	66-2500	15-180
Pseudomonas	25-2500	15-80
Streptococcus	200-2500	15-30
Escherichia	200-2500	30-120
Salmonells	1000-2500	15-60
Candida	3.75-2500	10-120
Enterobacter	1000-2500	60
Klebsiella	500-2500	60
Clostridium	1000	30-60
Corynebacterium	2500	60
Mycobacterium	2500	60-120

Uses of Povidone Iodine:

- As Skin Disinfectant:** The patient's skin is a major source of pathogens that cause infection. Traditional aqueous-based iodophors, such as povidone-iodine, are one of the few products that can be safely used on mucous membrane surfaces.⁶ PVP-I as 10% solution (1% available iodine) is widely used for skin disinfection and 7.5% PVP-Iodine solution (0.75% available iodine) is used for wound cleansing. The resultant broad spectrum of antimicrobial activity is well documented and its efficacy, particularly in relation to resistant micro-organisms such as methicillin-resistant *Staphylococcus aureus*, has been shown.⁷
- Pre Operative skin preparation:** Procedural and surgical site infections create difficult and complex clinical scenarios. A source for pathogens is often thought to be the skin surface, making skin preparation at the time of

the procedure critical. The most common skin preparation agents used today include products containing iodophors. PVP-Iodine products have been widely used for pre-operative skin preparation and in various surgical procedures and shown to significantly lower subsequent infection rates.⁸ In the aqueous form, most commercially available iodophors require a 2-step application in a scrub-and-paint technique, and their activity is limited by the amount of time the agent is in contact with the skin.⁹

- iii. Topical Application:** PVP-I in the form of ointments, sprays, lotions is used to prevent microbial contamination of wounds, ulcers, burns etc. PVP-Iodine effectively controls bacterial growth and protects the developing epithelium. Unlike many antibiotic agents it has the added advantage in that its continued use does not result in the generation of resistant organisms.¹⁰

Table 2: The topical application of different PVP-I preparations and their uses:

Application	PVP-I Preparation
Pre and post-operative antiseptic skin cleanser for major and minor surgical procedures.	Topical Solution 10% w/v Topical Alcoholic Solution 10% w/v Where quick drying effect is required
Skin cleanser for treatment of acne vulgaris, General disinfection of the skin.	Liquid Soap 4% w/v
Quick drying antiseptic for the treatment and prevention of infection. Useful against herpes simplex, herpes zoster, grazes, abrasions, cuts and wounds.	Antiseptic Paint 10% w/v
Treatment and prevention of infection in minor cuts and abrasions, minor surgical procedures and small areas of burns.	Ointment 10%w/v Dry Powder Spray 2.5% w/v
Treatment of infections in decubitus and stasis ulcers.	Ointment 10%w/v Dry Powder Spray 2.5% w/v
Antiseptic skin cleansers for pre-operative scrubbing and washing by surgeons and theatre staff and preoperative preparation of patients' skin.	Surgical Scrub 7.5% w/v with non-ionic surfactants

Oro-Dental Uses:

i. Anti-Caries Action: For prevention of dental caries, *S. mutans* numbers must be reduced and prevented from returning to the original level. An antibacterial agent that is effective and also acceptable to young children can help to establish a favorable oral environment and halt the caries process. In children suffering from early childhood caries, 10% povidone iodine applied in 3 month intervals over a period of one year has resulted in significant reduction in the rise of *Streptococcus mutans* levels decreasing the oral load of the organisms. Reduction in counts; in turn decreased the relapse of caries in these children.^{11,12}

ii. Pre-procedural Rinse: Antimicrobial mouth rinses used by patients before a dental procedure are intended to reduce the number of microorganisms released by a patient in the form of aerosols or spatter that subsequently can contaminate equipment, operator surfaces, and dental health care personnel. Pre-procedural rinse with povidone iodine can reduce the level of oral microorganisms generated in aerosols or spatter during routine dental procedures with rotary instruments (e.g., dental handpieces, ultrasonic scalers).¹³ Antimicrobial mouth rinses used by the patient before a dental procedure can decrease the number of microorganisms introduced into the patient's bloodstream during invasive dental procedures. The scientific evidence is not clear concerning the incidence and nature of bacteremia from invasive dental procedures, the relationship of bacteremia to disease, and the preventive benefit of antimicrobial rinses. However, the American Heart Association suggests that patients at risk for bacterial endocarditis use an antimicrobial mouth rinse before dental treatment.¹⁴

iii. Anti-plaque action: Povidone iodine appears to have no significant plaque inhibitory activity when used as 1% mouthwash and 30 to 40 % overall reduction in aerobes and anaerobes occurred with the active preparation which was significant.¹⁵ The absorption of significant levels of iodine through the oral mucosa may make this compound unsatisfactory for prolonged use in the oral cavity. Also, it could cause a problem of iodine sensitivity in sensitised individuals. This property combined with reversible staining and unpalatable taste made PVP-I disadvantageous when compared to Chlorhexidine and essential oil mouth washes.

iv. Endodontics: The essential role of microorganisms in the development and perpetuation of pulp and periapical diseases has clearly been demonstrated in animal models and human studies. Application of PVP-I solution as an endodontic irrigant was proposed based on its rapid antiseptic action against a broad range of microorganisms, low toxicity, hypoallergenicity, and greatly reduced tendency to stain dentin than other iodine containing antiseptics.¹⁶ 10% PVP-I is often employed for tooth surface disinfection and operating field which includes tooth, rubberdam and clamp. Fungi may be involved in cases of persistent and secondary infections associated with recalcitrant periradicular lesions; therefore the spectrum of antimicrobial activity of endodontic medicaments and irrigants should include these organisms. 2% PVP-I 4% killed all *C albicans* cells within 30 seconds, and a 10-fold dilution showed complete killing within 5 minutes.

Effect on fibroblasts: The fibroblast is the predominant cell type in the soft connective tissues of the periodontium and consequently plays a central role in normal function and in pathologic alterations. PVP-I has shown dose dependant reduction in cellular proliferation of fibroblasts. It was also seen that at dilute concentrations Povidone-Iodine showed insignificant effect on fibroblasts.¹⁷

Comparison with Chlorhexidine: Numerous studies exist in the literature comparing PVP-I with Chlorhexidine. In surgical site asepsis, PVP-I was found to be more effective in controlling the infection. However Chlorhexidine-alcohol was significantly more protective than povidone-iodine against both superficial incisional infections and deep incisional infections but not against organ-space infections.¹⁸ PVP-I lacks the persistent action of chlorhexidine but is less toxic and can be safely used in areas with ulcers and burns. PVP-I has broader microbicidal property especially on resistant bacteria like *M tuberculosis* and other spore forming bacteria. Protein-rich biomaterial and other organic materials can neutralize the germicidal activity of povidone-iodine, where as they have little effect on the antibacterial activity of chlorhexidine.

Conclusion: Since its discovery Povidone Iodine remains a commonly used disinfectant, and has been widely used in its different forms. The highly soluble nature, low toxicity, widest bactericidal range has made it a trusted agent in maintaining asepsis. The

recent emergence of single wall carbon nanotubes coated in a monolayer of povidone-iodine and its effect on wound healing holds a promising future for this compound.

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