

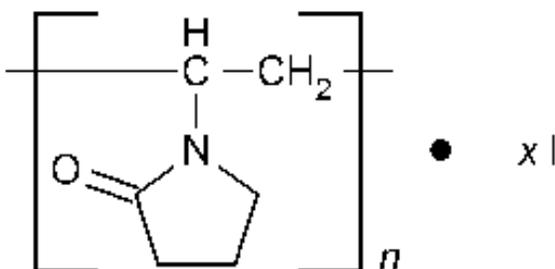
APPLICATION OF BROAD SPECTRUM ANTISEPTIC POVIDONE IODINE AS POWERFUL ACTION: A REVIEW

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1. Introduction:

Povidone iodinated is a complex of iodine and povidone. It contains not less than 9 % of available iodine¹.



2. Powerful action:

There are also reports available stating that PVP-iodine is effective as an antiviral too .numerous in-vitro studies made over two decades indicate the efficiency of PVP-iodine as a therapeutic agents for both humans and animals eleven products containing PVP-iodine were tested for their ability to inactivate HIV virus in cell culture system all of the products completely inactivated the virus at PVP iodine concentration greater than 0.5 % .usage PVP iodine has significantly reduced the irritancy and toxicity associated with iodine use its being used worldwide effectively³.

Povidone iodinated is a complex of iodine and povidone.it contains not less than 9% and not more than 12% of available iodine from this complex iodine

is released for prolonged time, concentration range of PVP-iodine between 3.75 -2500ppm kill the Candida strain between 10 to 120 seconds.

PVP-iodine and their preparation are official in USP, European pharmacopoeia and are recognized as effective broad spectrum biocidal agent the invitro biocidal activity has been studied for years against bacteria, yeast, moulds, viruses, fungi, protozoa, actinomycetes and rickettsia².

Eleven product contain PVP-iodine were tested for their ability to inactivate HIV virus in cell culture system. All of the products completely inactivated the virus at PVP-iodine concentration greater than 0.5%.Usage of PVP-iodine has significantly reduced the irritancy and toxicity with iodine use, and thus being used worldwide effectively³.

Compared to other preparations PVP-iodine exhibits markedly lower oral toxicity. Consequently, the accidental ingestion of PVP iodine solution is much less hazardous that from equal amounts of available iodine solutions. For this reason, PVP-iodine solutions do not require the hazardous, poisonous warning labels on bottle that iodine products must have. Moreover, animal and exposure tests have revealed virtually no skin reactions to PVP-iodine, and only very mild transitory effects on mucous membranes.

Candida species have become a major opportunistic pathogen causing recurrent oral thrush and oropharyngeal candidiasis. One third of healthy person with OPC symptoms will have an oral cavity culture that is positive for Candida albicans, the most common species for oral candidiasis. This has resulted in frequently high use of expensive antifungal drug like (clotrimazole, amphotericin B, fluconazole, itraconazole, ketoconazole and nystatin) which most of these patients mentality and they look for cheap and best prolonged effective drugs to manage this problem. The medical cost of care using PVP-iodine was very low compared with antifungal care.⁵⁰

3. General properties:

Povidone iodine was introduced to the pharmaceutical market as an antiseptic agent in the fifties and is as effective as iodine itself against a broad spectrum of disease-causing microorganisms. It differs from iodine in that it is less irritating to the skin and does not require iodides or alcohol to dissolve. Additionally, povidone iodine stains are water-washable. Early promotional materials refer to PVP iodine as "tamed iodine" because of its safety. Furthermore, the poison label required for iodine products are not necessary in commercial preparations containing PVP iodine.

- ◆ Broad spectrum biocidal activity
- ◆ detoxified iodine
- ◆ No detectable vapour pressure
- ◆ Water soluble
- ◆ Film forming capacity
- ◆ Stable complex

At the same time, PVP iodine is safer and easier to use than classic iodine preparations and has low system toxicity. The prolonged non-selective antimicrobial action of PVP iodine is unparalleled for surface microbiocidal activity and particularly effective in treating mixed infection. Its effectiveness has been clinically proven for all types of topical applications in both human and veterinary medicine⁹.

4. Action:

PVP iodine is a loose complex of elemental iodine with a neutral, amphipathic organic compound, polyvinyl pyrrolidone, which serves as a sustained release reservoir of iodine. The carrier augments dispersibility and penetrates. Povidone iodine is a topical microbial antiseptic which essentially retains the broad spectrum activity of iodine, yet is virtually free from the undesirable features associated with tincture of iodine and Lugol's solution. Iodine is bactericidal, sporicidal, fungicidal, protozoacidal, cysticidal and virucidal, gram-positive and gram-negative bacteria are about equally affected¹².

5. Pharmacology:

Elemental iodine has a very broad antimicrobial spectrum: bacteria, viruses, bacteria endospores, fungi, and protozoa's are destroyed through oxidative interaction and direct iodination of biological macromolecules. However, there have been reports of certain resistant germs. Povidone-iodine (synonym-PVP-iodine) is an iodophor, i.e. it is a labile complex of iodine with the polyvinylpyrrolidone, from which iodine is continually delivered. Only this

free iodine has antimicrobial activity. In iodophors there is a complex relationship between the concentration of the solution and the concentration of free iodine, so that e.g. through the dilution of a 10% solution with a rate of 1:10 more free iodine is released from the complex and the antimicrobial activity is increased.

6. Indications:

Povidone-iodine solutions in water or alcohol are better tolerated than iodine solutions with comparable efficacy. Considering the necessary time of application and the correct dilution povidone-iodine is suitable for hand disinfection, surgical hand disinfection, as well as preoperative and pre-puncture skin disinfection. However, compared to chlorhexidine the latter is normally more effective.

Povidone-iodine is further more used for the treatment of burns and of different lesions decubitus and leg ulcers etc). Specialist's opinions are divided on the indications. In any case, silver sulfadiazine is more effective for burns. In special preparations it is available for the therapy of inflammations in the mouth and pharynx and for vaginitis. For these indications there have only been limited comparisons with alternatives. Candida or trichomonal infections of the vagina undoubtedly better treated specifically. The use of povidone – iodine is particularly disputed for the irrigation of cavities¹⁵.

7. Contraindications:

Hypersensitivity to iodine, thyroid diseases, renal failure, burns covering

large surfaces (more than 20% of the body surface) pregnancy, nursing, and neonates than 6 months⁸.

8. Cautions:

All povidone – iodine preparations also contain a detergent in addition to the agent little is known about the tolerance of the detergents⁸.

9. Adverse Reaction

Severe complications are rare and only infrequently occur following application on intact skin. Extended long term treatment and repeated irrigation of wounds and cavities can provoke abnormal thyroid gland function, hepatic or renal insufficiencies, metabolic acidosis, chemical peritonitis, convulsions, Neutrogena, etc. The plasma concentration of thyroid gland hormones can rise. In infants one must expect considerable iodine resorption and the respective consequences following application on the skin local irritation with a burning sensation and pruitus occasionally occur, contact eczemas are rare⁸.

10. Interaction:

Concomitant administration of silver sulfadiazine or chlorhexidine partial inactivation possible⁸.

11. Stability: PVP-iodine can be stored in powdered form without significant iodine loss. Samples kept for three years at 65 C in glass stoppered bottle without tape or seal showed only 0.5% maximum loss of available iodine. The product should however be protected from moisture.

Published data show the stability PVP-iodine solutions are vastly superior to that of iodine tincture or Lugol's solution.

12. Compatibility:

PVP-iodine dosage forms have been compounded successfully as powders, tablets, liquid lotions, ointments, gels and sprays. If the vehicle or base reacts with iodine then the available iodine in the final preparation must be determined, since the germicidal activity of the finished product is dependent on the iodine, not the iodide content.

PVP-iodine systems should be mildly acidic since alkaline solutions, including ammonia, and reducing agents lower the available iodine which in turn, results in lower antiseptic activity pvp- iodine is compatible with steel, wool and plastic but reacts with silver.

13. Biocidal Activity:

For many years iodine has been recognized as an effective broad-spectrum biocidal agent. Using PVP-iodine has significantly reduced the irritancy and toxicity associated with its

use. Because of the products wide usage and established efficiency, it is presently included as an antiseptic agent in the United States pharmacopoeia as well as in many other national compendia.

Biocidal agents have been classically measured for effectiveness by the use of intro methods. In vitro results however should be considered only as preliminary measures of "cidal" efficacy. Factors such as skin penetration and reactivity can completely reverse any effectiveness rating determined by purely in vitro test methods.

The invitro biocidal activity of PVP-iodine has been studied for years against bacteria, yeast and molds. Actinomycetes and rickettsia. Activity of PVP-iodine versus bacteria, yeast, molds. Actinomycetes and rickettsia

Activity of PVP iodine Vs organisms (No. Strains)	Range of PVP iodine in ppm available iodine	Contact of kill time in sec.
Proteus(41)	100-2500	15-180
Staphylococcus(36)	66-2500	15-180
Pseudomonas(36)	25-2500	15-900
Streptococcus(25)	200-2500	15-30
Escherichia(23)	200-2500	30-120
Salmonella(9)	1000-2500	15-60
Candida(8)	3.75-2500	10-120
Serralia(6)	200-2500	60-120
Spores-baccillus;clostridium(6)	10,000	2.5hours
Trichomonas(5)	400-2500	30-60

Enterobacter(4)	1000-2500	60
Klebsiella(4)	500-2500	60
Clostridium(4)	1000	30-60
Shigella(3)	1000-2500	60
Corynebacterium(3)	2500	60
Diplococcus(3)	1000-2500	60
Mycobacterium(3)	1000-2500	60-120
Bacillus(3)	7.5-1000	10-30
Sarcina(2)	500-2500	60
Trichophyton(2)	1000	60
Aspergillus(2)	1000	30
Mima(1)	2500	60
Herella(1)	2500	60
Edwardsiella(1)	2500	60
Citrobacter(1)	2500	60
Providencia(1)	1000	60
Acinetobacter(1)	3.75	10
Epidermophyton(1)	1000	60
Microsporum(1)	1000	60
Pencillium(1)	1000	30
Nocardia(1)	2500	60

15. In vivo Studies

There have been reports that PVP iodine is effective as an antiviral agent.

14. Anti HIV

Eleven products containing PVP – iodine were tested for their ability to

inactivate human immunodeficiency virus (HIV) in a cell culture system. All of the products completely inactivated the virus at PVP – Iodine concentrations greater than 0.5% except for the lubricating antiseptic gel which required 2.5% Douche and Medicated douche products did not inactivate HIV at the concentrations prescribed for usual clinical use (0.33% and 0.25%, respectively) but were effective at PVP-iodine concentration of 0.5%.

Numerous in vivo studies made over approximately 35 years as well as the widespread clinical use of products containing PVP-Iodine as a therapeutic agent for both humans and animals. Following are some of the published

paper's supporting the clinical effectiveness of PVP-Iodine.

17. Health Hazards:

Acute: It is safe if used as a topical antimicrobial agent. Over exposure may cause local irritation to the skin can be absorbed through broken skin or lungs.

High concentration in blood may cause thyroid disorder, renal disturbances, Acidosis and electrolyte disturbances.

18. Precautions:

Spills should be cleaned as soon as possible wash affected area with dilute ammonia (or) dilute sodium thiosulfate solution and large amount of water.

Avoid breaking vapours (or) mists. Do not get in eyes, on skin (or) on clothing. / Wash thoroughly after handling and before eating (or) drinking. Removing contaminated clothing promptly.

Keep out of reach of children.

19. Emergency First Aid:

Eye – immediately wash with running water for 5 minutes. Get medical attention if irritation persists. Skin – avoid prolonged contact with excess wet solution. If irritation develops, get medical attention, ingestion – if swallowed, do not induce vomiting. Drink several glasses of water or milk. Obtain immediate medical attention. In half – if fumes cause respiratory discomfort, move to fresh air.

New Application:

Treatment of wounds:

PVP – Iodine Topical Solution (10% PVP Iodine containing 1.0% available iodine) is effective for ridding and preventing infections, including and preventing infections, including those with severe ulceration^{16, 17}.

Scrub and skin disinfection:

PVP – Iodine surgical scrub is a 7.5% PVP – Iodine solution (0.75% available

iodine) containing various agents for wound and skin cleansing. It should be rinsed off immediately after use to minimize skin irritation and healing retardation.

To reduce germs on skin and prevent infection in skin, the PVP- Iodine Topical solution containing 10% PVP-Iodine (1% available iodine) should be used. The PVP iodine film should remain on the skin so that it can act as a continued antimicrobial barrier.

To measure the efficacy of surgical scrubs, samples of scrub juices were taken to establish immediate, cumulative and persistent effects. The immediate effect is the reduction of bacteria found immediately after scrubbing .A cumulative effect is seen when regular use of the scrub leads to increasing reductions of bacteria .The final measurements persistence of effect , is defined as a decline in the post wash bacterial count . Studies with PVP-Iodine scrubs showed an effective, extensive immediate effect, a definite cumulative effect, and a persistence of effect^{18, 19}.

Preparation of the skin, pre-surgery

Numerous studies indicate the efficiency of PVP-iodine for presurgical skin preparation^{20,21}. There is even evidence that is effective against skin spores²².

Skin Burns, Abrasions and Infections:

Topical PVP-Iodine Antiseptics, Aerosol Sprays, Ointments (5% PVP-Iodine, 0.5% available iodine) and creams (5% PVP-Iodine, 0.5% available iodine) have been used to prevent microbial

contamination in burns, incisions and infected ulcers^{23, 24}.

Unlike iodine products, PVP- Iodine preparations may be bandaged.

These products should not be used on deep wounds or serious burns without consulting a physician. Use should be discontinued if redness, irritation, swelling or pain persists or increases.

Scalp, Vaginal and Throat Infections:

Shampoo containing 7.5%PVP Iodine has been reported to yield a significantly larger reduction of the germ count in the scalp and hair than products without PVP Iodine²⁵.

Douche and vaginal suppositories containing 10% PVP Iodine has been reported effective in the treatment of vaginal infections.

A mouth wash /gargle product containing 0.5% PVP Iodine is effective in reducing odour causing bacteria^{26, 27}.

For various surgical procedures:

PVP-Iodine products have been widely used in various surgical procedures and shown to significantly lower subsequent infection rates^{28, 29}.

Veterinary Medicine:

PVP-Iodine products have been used topically in the treatment of various swelling, chronic inflammatory conditions, sprains, bruises, obstinate ulcers, and to disinfect the umbilical stump of foals and calves. Because of its low toxicity and highly effective antimicrobial activity, topical PVP-Iodine applications have particular advantages in treating skin infection of cats, dogs, or

other animals that lick wounds .PVP-Iodine has also been found to be highly effective in treating bacterial and fungal fish eggs, thereby increasing the hatching yield. Additionally, scrub and antiseptic solutions containing PVP-Iodine have been reported as highly effective for use on dogs, cats and horse s for various pre-surgical procedures³².

Medical Equipment:

PVP-Iodine has been reported as an effective disinfectant for such diverse items as contact lenses, dialysis equipment, fiberscope, endoscopes, and a wide variety of dental and medical equipment^{33, 34}.

Toxicology

Compared to other preparations, PVP-Iodine exhibits markedly lower oral toxicity. Consequently, the accidental ingestion of PVP-Iodine solutions 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. Moreover, animal and human exposure tests have revealed virtually no skin reactions to PVP-Iodine, and only very mild transitory effects on mucous membranes'.

These results are in marked contrast to the effects of elemental iodine, which is a primary irritant and sensitizer. Preparations containing elemental iodine with no PVP frequently delay the healing of wounds by inhibiting formation of granulation tissue. PVP-Iodine is unique in effectively minimizing or eliminating these undesirable effects.

It may be left in contact with tissue for extended periods of time with no ill effects. Even bandages are permissible, whereas ordinary iodine preparations are not bandaged because the iodine sublimes onto protective covering causing pronounced irritancy to the tissue.

Safety and Efficacy

Toxicity test results, as well as usage for various medical conditions during the past approximate 35 years on many thousands of patients, all point to the safety and efficacy of products containing PVP-Iodine.

Advantages

- Stable complex
- No general odour
- No loss of iodine

- Rapid action even in presence of organic matter such as blood, pus, oil, grease, soap, etc.
- Film forming capacity
- Prolonged germicidal action
- Adheres to treated surface where applied colour delineates treated area.
- Water soluble so ease for formulation
- Non staining
- Low animal and phytotoxicity
- Non irritating to skin and mucous membranes
- Non sensitizing
- Non stinging
- It has reduced amount hazard
- Broad spectrum antiseptic
- Unparalleled for surface sterilization and in mixed infections.

No	Formulation	Application
1.	PVP iodine dermal solution 5% ¹⁷	Wounds and burns, pre-operative preparation of skin, mucous membrane, emergency microbial treatment of wounds, cuts and laceration skin
2.	PVP iodine surgical scrub 7.5% ¹⁸	disinfection in surgical procedure
3.	PVP iodine hand cleaners liquid 7.5% ¹⁹	Mild and gentle hand cleaner with iodine bactericidal activity
4.	PVP iodine liquid soap 7.5% ²⁰	antiseptic
5.	PVP iodine shampoo 4% ⁴²	Antidandruff seborrhea scalp condition
6.	PVP iodine ointment 10% ²³	Boils, furunculosis, impetigo, sycosis barbae otitis externa, paronychia, secondary infection of burns, wounds, fungi infection, taenia pedis corporis, cruris, versicolor, cutaneous candidacies.
7.	PVP iodine mouse wound dressing with allantoin 10% ²⁴	Infected skin lesion, burns
8.	PVP iodine cream 5%	infections
9.	PVP iodine vaginal gel 10%	Vaginal infection
10.	PVP iodine vaginal tablets 200 mg	Candidial trychomonal non-specific vaginitis
11.	PVP iodine vaginal douche 10%	Candidial trychomonal non-specific vaginitis
12.	PVP iodine vaginal suppositories 10%	candidiasis
13.	PVP iodine gargle 1%	acute oral mucosal infection

14.	PVP iodine dusting power 5%	infected skin lesion, exudative wounds, post surgical dressing, episiotomy
15.	PVP iodine aqueous spray with hydrocarbon propellant 5%	Topical antiseptic
16.	PVP iodine dry power aerosol spray 5% ²¹	Topical antiseptic
17.	PVP iodine swab sticks 10%	Topical antiseptic
18.	lotion 10%	Topical antiseptic
19.	PVP iodine aqueous spray with allantoin 5%	Topical antiseptic
20.	VC-kit 10%	Candidial trychomonal non-specific vaginitis

NO	Formulation	Application
21	Liposomal PVP Iodine formulation containing 4.5 to 5% PVP Iodine ⁴³	Viricidal efficosy as well as cytotoxicity effect
22	Liposomal Taurolidine & Povidone Iodine 0.01% ⁴⁴	Malignant pleural mesothelioma
23	Liposomal hydrogel with 3% PVP ⁴⁵	Antiinflammatory
24	Emulsions 4% PVP Iodine ⁴⁶	Topical Antiseptic
25	PVP Iodine gels as the lubricant ⁴⁷	Catheterization of the urinary bladder
26	Povidone Iodine gel 7.5% ⁴⁸	Anti microbial
27	IV solution of the Povidone Iodine diluted with the Ringers solution for reducing toxicity in the concentration of 0.23% ⁴⁹	Anti viral & Pathogenic H5N1 Avian influenza

Acquired Immune Deficiency Syndromes 2:16-20(1989)³

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