Iodine Compounds in Endodontics: An Update Review

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Iodine Compounds in Endodontics: An Update Review

LEARNING OBJECTIVES:
After reading this article, the individual will learn:

• The importance of iodine compounds in root canal treatment.
• Antibacterial and antifungal activity of iodine compounds against endodontic pathogens.

ABOUT THE AUTHORS

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Disclosure: Dr. Mohammadi reports no conflict of interest.

INTRODUCTION

Microorganisms and their by-products are considered to be the major cause of pulp and periradicular pathosis. Hence, the major objective in endodontic therapy is to disinfect the entire root canal system, which requires that all contents of the root canal system be eliminated as possible sources of infection. This goal may be accomplished using mechanical instrumentation and chemical irrigation, in conjunction with medication of the root canal system between treatment sessions. In order to reduce or eliminate bacteria, various irrigation solutions have been used during treatment. Iodine compounds can be used during treatment as a root canal irrigant and intracanal medicament. These compounds have a wide range of antimicrobial activity. The purpose of this article is to review the composition, mechanism of action, clinical applications, and related aspects of iodine compounds in 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. The elimination of microorganisms from infected root canal systems is a complicated task. Numerous measures have been described to reduce the number of root canal microorganisms, including the use of various instrumentation techniques, irrigation regimens, and intracanal medicaments. There is no solid evidence in the literature that demonstrates that mechanical instrumentation alone results in a bacteria-free root canal system, and when the complex anatomy of the root canal system is considered, this is not surprising. Further, there is in vitro and clinical evidence that mechanical instrumentation leaves significant portions of the root canal walls untouched, and complete elimination of bacteria by instrumentation alone is unlikely to occur. On the other hand, according to Ruddle, the Pro Taper rotary instrumentation system produces a centered preparation and contacts a significant portion of the internal walls of the canals.

It is assumed, but not demonstrated, that any pulp tissue left in the root canals can serve as nutrient for any remaining bacteria. Furthermore, tissue remnants also impede the antimicrobial effects of root canal irrigants and medicaments. Therefore, some form of irrigation and disinfection is necessary to remove residual tissue and to kill microorganisms. Chemical treatment of the root canal system can be arbitrarily divided into irrigants, canal rinses, and interappointment medicaments. Iodine compounds are used widely as an endodontic irrigant and medicament, but there has not been an adequate review of the literature regarding iodine compounds.

STRUCTURE AND MECHANISM OF ACTION

Iodine was first discovered in seaweed in the early 1800s and was shortly thereafter used to treat thyroid disease. In subsequent years, clinicians used iodine to treat almost every disease that failed routine treatment, including syphilis, lupus vulgaris, eczema, and psoriasis. Iodine is rapidly bactericidal, fungicidal, tuberculocidal, viricidal, and sporicidal. Its exact mode of action is not fully known,
however, it is thought that iodine attacks key groups such as proteins, in a concentration of at least 5 mg/L. Aqueous iodine solutions are unstable, with molecular iodine ($I_2$) being responsible for the antimicrobial activity. Iodophors (iodine carriers) are complexes of iodine and a solubilizing agent or carrier.\(^9\)

**Povidone iodine (PVP-I)** is an iodinated polyvinyl polymer. PVP-I consists of elementary iodine bound to the carrier poly-(1-vinyl-2-pyrrolidone). It is thought to induce cell death nonspecifically due to the oxidizing effects of free iodine on SH-, OH-, and NH- groups of amino acids and on double bonds of unsaturated fatty acids. The antibacterial properties and uses of PVP-I in medicine are well established.\(^9\) The natural element, iodine, has been used for more than 150 years in mucosal antisepsis, in the therapy of skin infections and burns, and in wound management. Yet, only after the introduction of PVP-I in the 1960s was it possible to employ this highly efficient microbicide to a wide variety of bacterial, fungal, and viral infections. PVP-I is water-soluble, does not irritate healthy or diseased oral mucosa, and exhibits no adverse side-effects such as discoloration of teeth and tongue and change in taste sensation, as seen with chlorhexidine. PVP-I has the potential to induce hyperthyroidism due to excessive incorporation of iodine in the thyroid gland, and should therefore be used only for short periods of time. Contraindications are patients with iodine hypersensitivity and thyroid pathosis, as well as pregnant and nursing women in order to protect the infant.\(^10\)

PVP-I is an effective material, as an adjunct, to treat periodontal infections (10% concentration for a contact time of at least 5 minutes). Furthermore, because of its antibacterial, antifungal, and antiviral properties, PVP-I is potentially useful in treating human immunodeficiency virus-related oral infections. Betadine (PVP-I 10%) (Purdue Frederick Company) and Betadine Scrub (a povidone-iodine solution that contains detergent) (Purdue Frederick Company) are leading antiseptics in US hospitals today.\(^11\)

**Potassium iodide (KI)** is a compound made of 76% of iodine and 23% of the alkali metal potassium, by weight. KI is prepared by reacting iodine with a hot solution of potassium hydroxide, the product being subsequently reduced to iodide by heating the dry reaction mixture with carbon. Another form of iodine compounds is iodine-potassium-iodide (IKI). The solution can be prepared by mixing 2 g of iodine in 4 g of KI; this mixture then is dissolved in 94 ml of distilled water.\(^12\)

**ANTIBACTERIAL ACTIVITY**

Several studies have evaluated the antimicrobial efficacy of different iodine compounds against root canal infections. 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.\(^13\) In 2 series of root canal treatment involving 1,304 and 3,069 teeth performed by undergraduate students, Engström, et al\(^14\) reported persisting microorganisms in 49% and 41% of the cases, respectively, after the use of 5% IKI. According to Möller,\(^15\) depending on the rate of fluid exchange, the effect of IKI may be expected to persist from one to 3 days. Safavi, et al\(^16\) showed that in 2% IKI-treated root canals in human teeth, a period of one to 2 hours was required to prevent growth of *Enterococcus faecium* in dentinal tubules, while the calcium hydroxide Ca(OH)$_2$ specimens still had positive cultures after 24 hours.

Molander, et al\(^17\) failed to demonstrate an enhanced antibacterial effect by combining 5% IKI for a period of 3 to 7 days with a subsequent 2-month period of Ca(OH)$_2$ dressing in human teeth where the smear layer was not removed. When IKI was used, 44% of the 50 cases examined showed positive growth, while the addition of Ca(OH)$_2$ to IKI resulted in only 20% positive cultures. Peciuliene, et al\(^18\) studied the effect of Ca(OH)$_2$ medication for 10 to 14 days on 20 root-filled teeth with apical periodontitis. Bacteria were isolated in 16 of the 20 teeth prior to instrumentation and in 5 teeth after instrumentation and irrigation (with smear layer removed). The third sample taken after 5 minutes of irrigation with 2% IKI in 4% KI (2% IKI 4%) showed growth from only one canal.

Abdullah, et al\(^19\) showed that a 10% PVP-I solution resulted in 100% bacterial reduction after 30 minutes in an *E faecalis* planktonic suspension, and 30 minutes in an *E faecalis* biofilm model, while Ca(OH)$_2$ was unable to
achieve 100% bacterial reduction even after 60 minutes. In a model using bovine teeth infected with *E. faecalis*, Baker et al.\(^2^0\) showed that every iodine containing agent tested (2% IPI, 2% IKI plus Tween 20, 10% PVP-I, 10% PVP-I plus detergent) performed significantly better than 10% Ca(OH)\(_2\). The most effective irrigant was 2% IPI, with nearly total elimination of *E. faecalis* within 15 minutes, while 10% Ca(OH)\(_2\) failed to eliminate *E. faecalis* from any of the samples. There was also no residual effect of the iodine-containing medicaments.

Sirén et al.\(^2^1\) used *E. faecalis* infected bovine root blocks to test the effectiveness of one-day and 7 days incubation of medicaments. The 2% IKI medicament showed results with no growth up to 700 µm and 950 µm at one and 7 days. Cardoso et al.\(^2^2\) evaluated the effectiveness of 10% PVP-I for one, 5, 10, and 15 minutes and observed that this agent was bactericidal after one to 5 minutes for *Staphylococcus aureus*, *Escherichia coli*, *E. faecalis*, and *Bacillus subtilis* spores decontamination. De Souza, et al.\(^2^3\) showed that a 3-second treatment with 10% PVP-I was efficient for gutta-percha cone disinfection. In a study to investigate the bactericidal effect of PVP-I against *E. faecalis* and to determine its minimum inhibitory concentration, Shurrab\(^2^4\) found that it was highly effective, and its minimum active concentration was 1%, making it a potential irrigating agent in infected root canals.

In a randomized clinical trial, Kvist et al.\(^2^5\) compared antimicrobial efficacy of endodontic procedures performed in one visit (including a 10-minute interappointment dressing with 5% IKI) with 2-visit treatments (including an interappointment dressing with Ca(OH)\(_2\) paste). Results showed that residual microorganisms were recovered in 29% of the one-visit teeth and in 36% of the 2-visit treated teeth, which was not statistically significant. It was concluded that from a microbiological point of view, treatment of teeth with apical periodontitis performed in 2 appointments was not more effective than the investigated one-visit procedure. In a study to evaluate effectiveness of 3 root canal medicaments to eliminate *Actinomyces israelii* from infected dentinal tubules in vitro, Basson and Tai\(^2^6\) found that 2% chlorhexidine (CHX) is superior to IKI and Ca(OH)\(_2\) in its ability to remove *A. israelii* from infected dentinal tubules.

**TOOTH SURFACE DISINFECTION**

Möller\(^1^5\) successfully used IKI for tooth surface disinfection for the first time. In another study, Ng et al.\(^2^7\) evaluated the effectiveness of 2.5% sodium hypochlorite (NaOCl), and 10% IKI for disinfection of the operation field (tooth, rubber dam, and the clamp) using both culturing and polymerase chain reaction (PCR) methods. The operation field was treated by 30% hydrogen peroxide and either by 10% IKI or 2.5% NaOCl. No significant difference in the recovery of cultivable bacteria from various sites in either group was detected. However, detection of bacterial DNA was significantly more frequent from the tooth surfaces after iodine treatment (45%) than after NaOCl treatment (13%).

**ANTIFUNGAL ACTIVITY**

Fungi (or yeasts) constitute a small proportion of the usual oral microbiota, with *Candida* spp. being the most common of the fungi in both healthy (30 to 45%) and medically compromised (95%) individuals.\(^2^8\) Fungi have occasionally been found in primary root canal infections, but they are more common in filled root canals in teeth that have become infected some time after treatment, or in those that have not responded to endodontic treatment.\(^2^8\) Overall, the occurrence of fungi reported in infected root canals varies between 1% and 17%.\(^2^9\) 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. Thus, medicaments that have antifungal effectiveness may assist in the successful management of persistent or secondary endodontic infections caused by fungi.

Waltimo et al.\(^3^0\) evaluated the susceptibility of 7 strains of *C. albicans* to 4 disinfectants, namely IKI, CHX-acetate (0.5%), NaOCl (5% and 0.5%), and Ca(OH)\(_2\). Each solution was tested individually as well as in pairs using all possible pairs of these 4 disinfectants. All *C. albicans* strains tested showed similar susceptibility to the medicaments. They were highly resistant to Ca(OH)\(_2\), but the NaOCl and IKI killed all cells within 30 seconds and the CHX-acetate showed complete killing after 5 minutes. In a study to
evaluate the efficacy of 2% iodine-iodate solution as an intracanal medicament against C albicans, Valera, et al found that this medicament killed 50% of the fungi after 2 weeks. Peciuliene, et al found that 2% IKI 4% killed all C albicans cells within 30 seconds, and a 10-fold dilution showed complete killing within 5 minutes.

Iodine-Potassium-Iodide AND CALCIUM HYDROXIDE

Peciuliene, et al showed that a 2% IKI 4%-saturated Ca(OH)2 combination was significantly less effective than 2% IKI 4%. In another study, Haenni, et al found that the ability of Ca(OH)2 to raise the pH in the root dentin was maintained when using a mixture of Ca(OH)2 with IKI. Furthermore, they recorded no additive antiseptic effects between Ca(OH)2 and IKI. Sirén, et al found that additive benefits can be achieved by combining Ca(OH)2 with IKI. Fuss, et al showed that a Ca(OH)2 and IKI combination was effective against E faecalis in a bovine tooth model. Using human single-rooted teeth infected with E faecalis, Cwilka, et al showed that Ca(OH)2/iodoform/silicone oil was the most effective combination followed by 2% IKI/Ca(OH)2 and then Ca(OH)2.

BUFFERING EFFECT OF DENTIN

As with other medicaments, the presence of dentin and its components are responsible for different inhibitory patterns on the activity of the iodine solutions. Haapasalo, et al demonstrated that dentin powder effectively abolished the effect of 0.2% IKI 0.4%, while dentin powder had a very limited capacity to inactivate 2% IKI 4%, where it took only 5 minutes to kill E faecalis. Portenier, et al showed that hydroxyapatite caused little or no inhibition, whilst the collagen matrix in dentin effectively inhibited 0.1% IKI 0.2%.

CYTOTOXICITY OF IODINE COMPOUNDS

Barnhart, et al measured the cytotoxicity of 6 endodontic irrigants (NaOCl, IKI, Betadine scrub (BS), Ca(OH)2, chlorine dioxide (ClO2), and Dulbecco’s Modified Eagle Medium [DMEM] [positive control]) on cultured gingival fibroblasts using the CyQuant assay. Human gingival fibroblasts were grown in DMEM containing 10% fetal bovine serum at 37°C and 5% carbon dioxide. At confluence, cells were split, plated in 96-well plates and incubated for 24-hours to allow attachment. The results showed that IKI and Ca(OH)2 were significantly less cytotoxic than ClO2, NaOCl, and BS. In conclusion, IKI and Ca(OH)2 are well tolerated by human gingival fibroblasts. In a microscopic study, Severyns, et al found that PVP-I was a very irritating solution provoking secondary thrombosis.

Iwasaki, et al assessed the cytotoxicity of povidone iodine on cultured mammalian cells using cultured Chinese hamster lung cells (V 79 cells). Results indicated that cytotoxicity of PVP-I occurs in dose and treatment time-dependent manners and that PVP-I induced inhibition of DNA, RNA, and protein syntheses of cells, even by the treatment which caused no reduction of cell survival. In an in vitro study to evaluate cytotoxicity of PVP-I mouthrinse on human gingival fibroblasts, Wilken, et al found that cells were immediately fixed by 20% PVP-I. Cabral and Fernandes compared the effect of CHX and PVP-I on the long-term proliferation and functional activity of human alveolar bone cells. Results showed that CHX affected mainly cell growth, whereas the effects of PVP-I were observed mostly in alkaline phosphatase production and matrix mineralization, and suggested that CHX had a higher cytotoxicity profile than PVP-I.

ALLERGIC REACTIONS TO IODINE COMPOUNDS

The term iodine allergy has been defined generally as “an allergic reaction induced by the use of iodine-containing drugs” such as inorganic preparation used as a skin disinfectant or various organic iodine-containing drugs. Accordingly, it has generally been thought that iodine allergy is cross-sensitive to various iodine-containing chemicals. However, this concept seems to deviate from the immunological principle that immune recognition is specific. In order to solve this contradiction, it has been hypothesized that iodine allergy is an immunological reaction to iodinated autologous proteins produced in vivo by iodination reaction from various iodine-containing chemicals. Iodination of proteins by iodine occurs readily, even at physiologic pH. Allergic reaction to iodine compounds has
been reported as one of the major disadvantages of these compounds in endodontic literature.43

**CONCLUSIONS**

Iodine compounds are a group of important antiseptic and antimicrobial agents in the field of medicine and dentistry. Among them, IKI is the most acceptable compound in endodontics. It has a broad range of antibacterial and antifungal activity. It has also been used as a tooth surface disinfectant agent prior to root canal sampling. The synergistic (additive) antiseptic effects between Ca(OH)₂ and IKI are still controversial. Furthermore, the presence of dentin, especially its organic components (mainly collagen), has a buffering (inhibitory) effect on the antimicrobial activity of iodine compounds. It seems that cytotoxicity of iodine compounds is dose-dependent and low in the concentrations used in endodontics. Allergic reactions to iodine compounds, like other irrigation solutions, have also been reported. Considering the potential side effects of NaOCl (ie, toxicity) and the possibility to induce hypochlorite accident,44 iodine compounds may be considered as appropriate substitutes for NaOCl in cases with open apices and where the placement of a rubber dam is not possible.

**REFERENCES**


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2. The occurrence of fungi reported in infected root canals varies between:
   a. 1% and 17%.
   b. 30% and 45%.
   c. 60% and 80%.
   d. 1% and 3%.

3. According to Portenier, et al which of the following components of dentin has the weakest inhibitory effect on the antimicrobial activity of iodine compounds?
   a. Hydroxyapatite
   b. Type I collagen
   c. Type III collagen
   d. Type V collagen

4. Iodine-potassium-iodide (IKI) solution is prepared by mixing:
   a. 2 grams of iodine in 4 grams of KI and dissolving this mixture in 94 ml of distilled water.
   b. 4 grams of iodine in 2 grams of KI and dissolving this mixture in 94 ml of distilled water.
   c. 10 grams of iodine in 20 grams of KI and dissolving this mixture in 70 ml of distilled water.
   d. 25 grams of iodine in 25 grams of KI and dissolving this mixture in 50 ml of distilled water.

5. According to Sirén, et al intracanal medication with the 2% IKI showed no bacterial growth up to:
   a. 700 µm and 950 µm.
   b. 100 µm and 250 µm.
   c. 300 µm and 400 µm.
   d. 400 µm and 500 µm.

6. Antimicrobial action of iodine compounds occurs in a concentration of at least:
   a. 5 mg/L.
   b. 10 mg/L.
   c. 50 mg/L.
   d. 100 mg/L.

7. According to Baker, et al which of the following agents had lesser efficacy against Enterococcus faecalis?
   a. IKI plus detergent
   b. Povidone iodine (PVP-I)
   c. PVP-I plus detergent
   d. Calcium hydroxide

8. Safavi, et al showed that in 2% IKI-treated root canals in human teeth, a period of ____ was required to prevent growth of E faecalis in dentinal tubules.
   a. 1 to 2 hours
   b. 24 hours
   c. 48 hours
   d. 96 hours
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