### Comparison: Peridex®  DioxiRinse®  Listerine®

<table>
<thead>
<tr>
<th>Peridex</th>
<th>DioxiRinse</th>
<th>Listerine</th>
</tr>
</thead>
<tbody>
<tr>
<td>chlorhexidine</td>
<td>active chlorine dioxide, ClO₂</td>
<td>essential oils</td>
</tr>
<tr>
<td>Not safe to swallow, may cause stomach upset or nausea, eye injury 4, 7, 14</td>
<td>Safe for incidental ingestion. ClO₂ used in water purification. Many studies illustrate safety 42, 55, 56</td>
<td>Alcohol content may cause toxicity, critical for children 84, 85, 86</td>
</tr>
<tr>
<td>Highly unpleasant taste causes patient non-compliance 1, 4, 11, 12</td>
<td>Fresh, effervescent mint taste 57</td>
<td>Unpleasant taste. May cause non-compliance 70, 82, 83</td>
</tr>
<tr>
<td>Will not kill spores, small effect on fungi. Ineffective on Pseudomonas 27 Proteus, Serratia, Mycobacteria 8, 9, 10</td>
<td>Kills all bacteria, spores, viruses and yeast, in one minute, in vitro. Includes MRSA, C. difficile 38, 39, 40, 44, 64</td>
<td>Little evidence of an antibacterial effect in vivo or in vitro 65, 66, 68, 69, 75, 77, 79</td>
</tr>
<tr>
<td>Stains teeth, dentures, and dorsal area of tongue 1, 7, 11, 13</td>
<td>Will not stain teeth, dentures. Whitens teeth, removes biofilm 34, 36, 41</td>
<td>Does not stain or whiten teeth, not an oxidant</td>
</tr>
<tr>
<td>Prolonged use can cause calculus formation. Conflicting reports as to plaque reduction 1, 3, 12, 13, 17</td>
<td>No restrictions for use. Further reduces plaque when combined with SRP 29, 47, 52</td>
<td>Prolonged use may produce mucosal lesions. Little or no odor or plaque reduction 73, 74, 75, 76, 80, 87</td>
</tr>
<tr>
<td>Can damage mucous membranes and inhibit healing. Allergic reaction may cause mouth sores, white patches 10, 11, 14</td>
<td>Heals sores and irritations caused by dental procedures and braces 31, 43, 51, 53, 59</td>
<td>May cause gum or gingival pain 65, 70, 84, 86</td>
</tr>
<tr>
<td>Eating, brushing or drinking diminishes efficacy 7, 16, 21, 22</td>
<td>Odor removal and disinfection is immediate. Used daily any time 33, 37</td>
<td>Repeated use may cause oral burning sensation 70, 83, 89</td>
</tr>
<tr>
<td>Prevents wound healing, although often applied on wounds 10, 15, 23</td>
<td>Cures oral yeast infection, 32, 48, 49 Pseudomonas wounds, abrasions</td>
<td>Some reports on impairing wound healing 73, 74, 86</td>
</tr>
<tr>
<td>Can decrease taste sensation, and alter taste 4, 12, 13</td>
<td>No effect on taste. Used routinely as a mouthwash 57</td>
<td>Highly unpleasant mouthwash taste 65, 83</td>
</tr>
<tr>
<td>Good for mouth odor control, cannot be used routinely. Kills bacteria but does not oxidize VSCs 11, 12</td>
<td>Fastest neutralizer of odor and odor causing bacteria, oxidizes VSC and VSC proteins 33, 38, 42, 47</td>
<td>Masks, not neutralizes odor 73, 84, 88</td>
</tr>
<tr>
<td>Reports of anaphylaxis, renal, liver damage. Overdose has caused slurred speech in children 19, 20, 23, 26, 28</td>
<td>No adverse effects reported 32, 54, 56, 59</td>
<td>Few adverse effects, but no studies proving efficacy presented 65, 83</td>
</tr>
<tr>
<td>Alcohol content 11.7% 12</td>
<td>Alcohol content ½%</td>
<td>Alcohol content 27% “54 proof” Useful for dissolving oils 81,89</td>
</tr>
<tr>
<td>Recommended for gingivitis, but only with SRP (FDA). May mask and worsen periodontitis 2, 5, 6, 13, 15</td>
<td>Clinical evidence for alleviating gingivitis and periodontitis 46, 47, 50, 57</td>
<td>No improvement in plaque or gingivitis-despite marketing claims 67, 68, 76, 80, 85, 87</td>
</tr>
<tr>
<td>Incompatible with soaps, carbonate, chloride. Neutralized by hard water 21, 22</td>
<td>Incompatible with strong reducing agents which will neutralize ClO₂</td>
<td>No reported incompatibilities</td>
</tr>
<tr>
<td>Not indicated for mucositis, stomatitis due to membrane irritation 14, 15, 24, 25</td>
<td>Successfully treats mucositis, stomatitis, glossitis 32, 62</td>
<td>Does not alleviate mucositis stomatitis, alcohol drying effect 84, 86</td>
</tr>
</tbody>
</table>

**References Available**

References to Mouthwash Comparison Chart available on request

Peridex

1 Charles, CH, Mostler KM, Bartels LL, Mankodi SM, *J Clin Periodontology*, 2204 Oct; 31(10): 878-84, “The chlorhexidine mouthrinse group had significantly more calculus and extrinsic tooth stain than either the essential oil mouthrinse group or the control group… side effects associated with chlorhexidine mouthrinse may limit patient compliance.”

2 FDA Warning Letter to Zila Pharmaceuticals, Inc. 4/18/’08. “FDA is not aware of evidence that Peridex can heal gingivitis and prevent other forms of periodontal disease.” “A company brochure for the rinse, which is approved to treat gingivitis, also made unproven claims about how well Peridex worked and made false statements about competitors’ products.” “These claims as to the effectiveness of Peridex in the oral cavity are misleading because they are not supported by substantial evidence.” “Peridex is only indicated as part of a professional program for the treatment of gingivitis.” “The effect of Peridex Oral Rinse on periodontitis has not been determined.”… There is no evidence that Peridex has such effects with regard to overall health or serious medical conditions, including heart disease, stroke, uncontrolled diabetes, low protein births, and respiratory disease.” “The violations discussed in this letter do not necessarily constitute an exhaustive list.”


4 Drugs.com. Review of side effects of Peridex, Unpleasant taste, dry mouth, staining of teeth, white patches or sores, decreased taste sensation, swelling salivary glands, mouth ulcers. Keep medication out of eyes ears and mouth. Can cause allergic reactions, especially in genital area.

5 Mayo Clinic.com., Chlorhexidine drug information, Apr. ‘00 “Use of chlorhexidine may make other gum problems, such as periodontitis, worse.”

6 America’s Dental Bookstore, Peridex, “Peridex has been shown to be effective in treating gingivitis, but it has never been shown to have any effect on the more serious gum disease, periodontitis, in which the supporting structures of the teeth are affected.”

7 MedicineNet.com. Peridex side effects. “Staining of teeth, mouth irritation, mouth sores, stomach upset, nausea, allergic reactions, e.g. rash, itching, swelling. Do not rinse mouth, brush teeth or eat immediately after using this drug.”


9 HARI, “Disease Prevention Through Proper Sanitation and Disinfection in an Indoor Psittacine Breeding Facility,” “Pseudomonas grows well in standing water and chlorhexidine is ineffective against it.”

10 Salami AA, Imosemi IO, Owoeye OO, *Int. J. Morph.*, 24(4):673-676, ‘06. “A Comparison of the Effect of Chlorhexidine, Tap Water and Normal Saline on Healing Wounds” “Chlorhexidine causes damage to new tissues and should not come in contact with meninges and mucous membranes as this can cause permanent damage. Its antimicrobial efficicacy is not total, as certain microbes are known to grow in the solution; of note in this regard is *Pseudomas aeruginosa* and *Proteus mirabilis.* The presence of microbes in the wound which were probably brought by the antimicrobial agent, further contributed to the delayed healing seen in the antiseptic treated cases and also worsened the general state of the animals.” “…these agents should not be used on clean healing wounds.”

11 Rosenberg, M, *Scientific American*, Apr. ‘02, “The Science of Bad Breath” “--- effective against halitosis. Unfortunately, it can also discolor teeth, impair taste and generate oral ulcerations. These effects, though reversible, preclude the use of chlorhexidine for more than a few days.”

12 Dr. Dan Peterson, “Family Gentle Dental Care.” “Chlorhexidine may cause staining of teeth, increase in calculus formation, lingering taste causing possible change in taste perception. Contains 11.6% alcohol.”

13 DailyMed (http://dailymed.nlm.nih.gov/dailymed/droginfo.cfm?id=6210). “The effect of Peridex on periodontitis has not been determined. An increase in supragingival calculus was noted, staining of oral surfaces, alteration in taste perception, minor irritation and superficial desquamation of oral mucosa.”
Among postmarketing reports, the most frequently reported oral mucosal symptoms associated with chlorhexidine are stomatitis, gingivitis, glossitis, ulcer.

Although chlorhexidine gluconate topical oral solution has been used as an adjunct for the treatment of acute necrotizing ulcerative gingivitis, safety and efficacy of the oral solution for this use has not been established. "Safety and efficacy of subgingival chlorhexidine gluconate in acutely abscessed periodontal pockets has not been established to date and such use is not recommended."

There are no studies to date evaluating the comparative safety and efficacy of the various anti-infectives for subgingival administration that are commercially available in the US.

Do not swallow Peridex. If Peridex is accidentally swallowed, stomach upset or nausea may occur. "Do not rinse mouth, brush teeth or eat immediately after using Peridex." "Mouth sores may occur.

Do not eat or drink for several hours after using the oral rinse as this may decrease the effect of the medicine.

Chlorhexidine oral rinse will not prevent plaque or tartar from forming on your teeth...Do not eat or drink containing alcohol.

Chlorhexidine gluconate solution has been confirmed as the causative agent of type I hypersensitivity by intradermal, scratch, and epicutaneous tests; chlorhexidine may not be suitable for application to mucous membranes.

The potential risk of anaphylactic reactions due to the application of chlorhexidine is well known, especially that application to mucous membranes can cause anaphylactic reactions and was therefore discouraged.

Studies have shown that chlorhexidine is minimally active against HIV, and herpes simplex virus; is somewhat effective against fungi.
28 Lake APJ, *The Internet Journal of Anesthesiology* ‘07. Volume 13, Number 2. “Anaphylactic reactions associated with general anaesthesia though rare can be life threatening and caused by administered agents not directly connected to the anaesthetic. In this case a reaction, which was not immediately recognized as such, was most likely due to chlorhexidine.”

28a Hogan, JS, Smith KL, Todhunter DA, Schoenberger PS, “Animal Sciences Research and Reviews, Special Circular 156, Efficacy of a Barrier Teat Dip Containing 0.55% Chlorhexidine for Prevention of Bovine Mastitis.” “Cows dipped with the barrier in the current trial had a 52.1% increase in Pseudomonas spp. IMI. and a 49.9% in Serratia spp.IMI compared with incidence for cows dipped with the 1% iodophor. Both Serratia spp. and Pseudomonas spp. have been reported to contaminate chlorhexidine gluconate solutions.”

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**DioxiRinse**


30 Jay Youngerman, ENT Specialist, Letter, July 12, ‘02. “We have been very successful in using DioxiRinse in the treatment of Stomatitis, Glossitis, Gingivitis. We have also had success in the treatment of post radiation and chemotherapy oral lesions.”

31 Jay Youngerman, ENT Specialist, Letter Nov. 6, ‘02. “I have used DioxiRinse on patients who have extensive gum disease that seems to be causing problems with lypheadenopathy and with gum pain and bleeding. In general, I am very pleased with your products.”

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38 Westbury Diagnostics, Inc. Farmingdale, NY Aug. 7, ‘99. Microbial Challenge of Two Mouthwash Formulations, 10 logs of S aureus were killed in one minute by DioxiRinse Mouthwash.

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43 Abdel Mohammad, DDS MS MPH FACD Ohio State University, College of Dentistry, February 22, ‘01 “Study: The use of Chlorine Dioxide on immediate dentures and geriatric patients. “When the chlorine dioxide antiseptic system is used after the denture is inserted, it will enhance the wound healing process.”


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49 Kenyon AJ, Hamilton SG, Douglas DM. American Journal of Veterinary Research, Vol. 47, No. 5, pp.1101-1104. “Comparison of Antipseudomonad Activity of Chlorine Dioxide.” “In this model, the chlorine dioxide-containing gel was more active than were preparations of providine-iodine, chlorhexidine, or silver sulfadiazine.”

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58 Frank Feng, DDS. “I’d like to complement you on your fine mouthwash. We have been using it now for almost three years. Although I have no particular desire to get into sales, the surprisingly good results our patients have experienced, especially with bad gums, encourages me to do so. More than a handful of patients avoided seeing a Periodontist after conscientious use of DioxiRinse. The pleasant taste seems to help these patients maintain a good regimen. I’m surprised that chlorine dioxide “has not taken over the world.”

59 Milton Dines, DDS. “I have applied your ClO2 solution to a number of periodontal abscesses in the active stage. In the three instances there was improvement in the status of the abscesses without noticeable adverse side effects.”
60 Martin Dinnes, DVM. “Dental fistula in a white tiger. An epithelialized fistulous, infected tract responded in three days and closed completely following extraction of the offending tooth and three treatments with Citronex liquid. Tusk fracture in an elephant with abscessation and osteomyelitis of the adjacent alveolar bone. The daily use of citronex liquid and gel caused the infection to heal and a remission of the osteomyelitis. I feel that the animal might have lost his tusk were it not for availability and utilization of citronex.”

61 Silberman, MS, DVM “One unique case was an oral lesion in a black rhinoceros. This is a recurring lesion that has been almost impossible to handle medically. When treated with chlorine dioxide topically for a few days, the lesion was resolved.”

62 Rosemary Fish, DVM “We have used your chlorine dioxide both as a mouth flush and as a gel application in our snakes with stomatitis. This compound caused no noticeable irritation in snakes receiving daily treatment, and two animals which were treated recovered completely with no other therapy.

63 Ronald Feldman, MD “One patient used the solution to gargle with a severe sore throat with terrible pain. She had excellent relief of pain with half an hour.”

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**Listerine**

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89 NYTimes.com The Media Business, Jul. 1993, Ref. “Yet Listerine is predicated on its sometimes harsh taste, serving as a signal that it is powerful enough to freshen breath and kill germs—‘the taste people hate twice a day,’ ads proclaimed.”

77 Wikipedia Listerine ‘08 “The efficacy of the treatment is due mainly to Listerine’s liquid properties. By the same token, it doesn’t even meet the FDA standard to be listed as an antiseptic. See for yourself at the FDA’s web site.”

85 iVillage.com Total Health “Cosmetic mouthwashes have a limited effect on dental health. Although manufacturers tout over-the-counter mouthwashes as an effective way to promote oral health, dental experts generally do not believe that they offer significant benefits over simple flossing and brushing with a toothpaste containing fluoride. The effects are temporary.

84 Springen, Karen, Newsweek Apr. 24, 2008, “Critics of alcohol-containing products say that alcohol dried the mouth, which could potentially worsen breath. It is a carrier for essential oils that are the active ingredients in Listerine.” “Alcohol draws moisture out of the tissues, and also slows salivary flow,” says Laura Brinker a spokeswoman for Proctor & Gamble. says the ADA’s Richard Price. “After they bathe, people put on deodorant-just as they use mouthwash after they brush their teeth. The mouthwash is not as important as physically removing the bacteria. You don’t need a mouthwash says Richard Price.” “A dry mouth leads to an overgrowth of bacteria,” says Dr. Susan Karabin, president of the American Academy of Periodontology. “Children’s livers aren’t fully developed, so alcohol exposure can be toxic and even put them in a coma.”

86 Flemingson EA, Ambalavanan N, et.al. Indian Journal of Dental Research Vol. 19, Issue 1, pp.29-35.”It was seen that mouthrinses produced a significant improvement in the Gingival index (GI) after one month. Despite the improvement, the GI was still indicative of disease. No improvement in the Plaque index (PI) occurred in the essential oil group.”

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85 iVillage.com Total Health “Cosmetic mouthwashes have a limited effect on dental health. Although manufacturers tout over-the-counter mouthwashes as an effective way to promote oral health, dental experts generally do not believe that they offer significant benefits over simple flossing and brushing with a toothpaste containing fluoride. The effects are temporary. Mouthwashes are generally not recommended for use in children 12 and younger. There is the risk that children may swallow mouthwash instead of spitting it out. This can lead to alcohol poisoning, requiring medical attention.”

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87 Wikipedia Listerine ‘08 “The efficacy of the treatment is due mainly to Listerine’s liquid properties. By the same token, however, this treatment is ineffective at physically removing plaque buildup.”

88 NYTimes.com The Media Business, Jul. 1993, Ref. “Yet Listerine is predicated on its sometimes harsh taste, serving as a signal that it is powerful enough to freshen breath and kill germs—‘the taste people hate twice a day,’ ads proclaimed.”


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