

bicarbonate (Ref. 145) further reduces the likelihood of a mutagenic effect occurring with combination products.

A 1989 mutagenicity study by Kuhn et al. (Ref. 415) tested varying concentrations of a gel containing levels of hydrogen peroxide up to 100 µg/plate in a bacteriological assay for toxicity and mutagenicity on several strains of *S. typhimurium*. The results showed no toxic or mutagenic effects on the strains tested, which was approximately 100 times greater than the optimal mutagenic response seen with aqueous hydrogen peroxide. This result is in contrast to other studies using strains of *S. typhimurium* that showed mutagenic action associated with hydrogen peroxide (Refs. 163, 168, and 416). This result is also in agreement with studies conducted with peroxide formulated in dental products that are uniformly not mutagenic in oxidant-sensitive bacterial strains (Refs. 172 and 417).

After 1 minute of brushing, recovery of hydrogen peroxide in the presence of baking soda was less than 5 percent of the amount introduced into the oral cavity (Ref. 145). Identical results on hydrogen peroxide decomposition were seen in control subjects and subjects with impaired salivary flow.

Using a rat animal model, a combination of sodium bicarbonate and hydrogen peroxide incorporated into a toothpaste vehicle was tested for oral mucosa irritancy by Meyers et al. (Ref. 418). The particular formulation was found to be a mild-to-moderate irritant. However, the test toothpaste was found to be less irritating compared to a common fluoridated toothpaste used as a control. Unfortunately, the concentrations of ingredients did not appear to be listed, including the concentration of sodium bicarbonate and hydrogen peroxide. These results do not agree with those reported by Marshall et al. (Ref. 184), in which no irritation was found to the oral mucosa of hamsters administered a dual phase hydrogen peroxide and sodium bicarbonate dentifrice containing 0.75 percent or 1.5 percent hydrogen peroxide and 5 percent or 7.5 percent sodium bicarbonate once-daily, five times per week for up to 20 weeks.

Two animal studies examined the potential for oral mucosal irritation by hydrogen peroxide in combination with sodium bicarbonate (Ref. 184). No mucosal irritation was observed after administration of a hydrogen peroxide and baking soda dentifrice once daily, five times a week for 20 weeks. These results support clinical and consumer studies that show no evidence of oral irritation following use of dentifrices containing a combination of these

ingredients. A study by Kuhn et al. (Ref. 419) used a combination of 10 percent sodium bicarbonate and 1.5 percent hydrogen peroxide. The study included exposure of the test animals to DMBA, a known carcinogen, and evaluated if any of the test compounds (including this combination) resulted in additional carcinomas. The test and control compounds were administered in a 20-week cheek pouch mucosal irritation study and no additional carcinogenic effects from the test combination were found. These results and those seen in a second hamster bioassay (Ref. 184) are contrary to those of Weitzman et al. (Ref. 183) who found that, when combined with DMBA, hydrogen peroxide, only at a concentration of 30 percent, appeared to augment the carcinogenic effects associated with DMBA. No augmentation of the carcinogenic effects of DMBA was seen with 3 percent hydrogen peroxide in the Weitzman study (Ref. 183), whose results support the previous observations that concentrations of hydrogen peroxide of 3 percent or less are safe for use in the oral cavity.

In a 9-month human trial with concentrations of 10 percent sodium bicarbonate and 1.5 percent hydrogen peroxide used as a dentifrice, Truelove (Ref. 420) found no increase in yeast concentrations in test subjects compared to subjects using a standard fluoridated dentifrice.

There are reports in the literature of excessive use of these compounds producing marked gingival detrimental changes, although these lesions appear to be easily correctable (Refs. 421 and 422).

ii. *Effectiveness.* The value of the combination of hydrogen peroxide and sodium bicarbonate has led to a continuing debate within the dental research and clinical communities. An in vitro MIC and minimal bactericidal concentration (MBC) study found that both ingredients were weak bacteriocidal agents, with sodium bicarbonate requiring extremely high dosages to cause bacterial cell death (Ref. 423). Varying outcomes resulted from the concentration of ingredients, with some mixtures inhibiting/killing while other concentrations produced a synergistic effect. In one study, a combination of 3 percent hydrogen peroxide, 0.5 g of sodium bicarbonate, and 10 g sodium chloride was tested on 10 experimental and 10 control subjects who had moderate periodontitis and were carefully scaled and root planed at the beginning of the study (Ref. 424). The experimental subjects had the test ingredients administered at home with a toothbrush and at biweekly

professional irrigations. Sites in the test group also received iodine applications. The results indicated that following scaling and root planing, and with a carefully monitored oral hygiene regimen including sodium chloride and iodine in addition to the hydrogen peroxide and sodium bicarbonate, a reduction of several clinical periodontal parameters occurred after 3 months of treatment. This study suggested a significant effect on the oral flora could be achieved by subgingival irrigation with these chemicals.

In a 3-week study (Ref. 425), a 1.5-percent hydrogen peroxide and a 2-percent sodium bicarbonate mouthrinse was tested in a positive and negative parallel-control study. The results indicated significant control of gingivitis and gingival bleeding compared to the negative control. The rinse compared favorably to the positive control 1.2 percent chlorhexidine rinse. The Subcommittee found that the study only evaluated efficacy up to 3 weeks, and long-term results are unknown.

Using a split-mouth design, Greenwell et al. (Ref. 426) tested the effect of this combination (hydrogen peroxide, sodium bicarbonate, and salt water) against standard oral hygiene methods. The effects on commonly monitored indices suggested no significant effect over the standard oral hygiene control except where initial therapy was not instituted. However, these subjects were diagnosed with treated or untreated periodontitis, and the study was limited to 8 weeks.

In a similar study, four subjects with early periodontitis used either a fluoridated paste or an experimental paste containing 3 percent hydrogen peroxide and sodium bicarbonate in a splitmouth study design. Over the 3-week test period, no discernible differences between the groups could be identified (Ref. 427). Similar results were found in a 3-month study in which the test ingredients (hydrogen peroxide and sodium bicarbonate) were applied with a toothpick (Ref. 428).

In a 2-year study in which salts and hydrogen peroxide mixture was compared to conventional oral hygiene methods, no discernible differences could be found using phase contrast microbiological parameters (Ref. 429). In another 2-year study, no positive clinical effects were discernible from the use of the combination of test ingredients (hydrogen peroxide, sodium bicarbonate, and sodium chloride) compared to conventional oral hygiene methods (Ref. 430). The 4-year data from the same subject group showed the same results as seen at 2 years (Ref. 431). As in the study noted above (Ref.