

Alkyl dimethyl amine oxide and alkyl dimethyl glycine

Hydrogen peroxide and povidone iodine

Hydrogen peroxide and sodium bicarbonate

Hydrogen peroxide, sodium citrate, sodium lauryl sulfate, and zinc chloride

Peppermint oil and sage oil

Polydimethylsiloxane and poloxamer

Stannous pyrophosphate and zinc citrate

a. *Alkyl dimethyl amine oxide and alkyl dimethyl glycine.* The Subcommittee concludes that there is insufficient evidence to support the safety and effectiveness of the combination of alkyl dimethyl amine oxide and alkyl dimethyl glycine as an OTC antingivitis/antiplaque agent. This combination consists of two amphoteric (having both acidic and basic properties) quaternary ammonium inner salt surfactants said to have broad spectrum antimicrobial activity.

i. *Safety.* An acute oral toxicity study (Ref. 377) of a 3-percent solution of alkyl dimethyl amine oxide and alkyl dimethyl glycine calculated that the LD₅₀ in Sprague-Dawley rats was greater than 6,000 mg/kg. Necropsy observations included slight intestinal hemorrhage, slight liver discoloration, and slight to severe lung congestion.

An additional acute toxicity study in beagle dogs (Ref. 378) was difficult to evaluate because the dosages were stated in mL/kg but the concentration of the solution was not stated. Although there did not appear to be a constant pattern at necropsy, all of the dogs displayed abnormal findings, such as cortical congestion of the mesenteric lymph nodes, white nodules on the gall bladder mucosa, and consolidation of the lungs with a yellow-colored mucoid material in the bronchi.

A series of dermal toxicity studies was carried out. Again, because the concentration of the liquid used was not stated, these studies were difficult to evaluate. In one study (Ref. 379), the dermal toxicity of a 3-percent solution of the combination of alkyl dimethyl glycine and alkyl dimethyl amine oxide was evaluated on abraded skin of rabbits. Two of 20 animals displayed minimal reaction. An additional study (Ref. 380) reported that 3.6 percent of an applied dose was absorbed through rabbit skin.

Two dermal sensitization studies were carried out in guinea pigs (Refs. 381 and 382) and appeared to have diverse results. In one study (Ref. 381), the investigator concluded that there was no evidence suggesting the combination of these ingredients can act as a sensitizer in the guinea pig.

However, it was unclear what concentration of the test material was used. In the second study (Ref. 382), it was concluded that repeated topical exposures of guinea pigs to a 3-percent solution of these ingredients has the potential to induce mild dermal sensitization.

Based on the results of a *Salmonella*/microsome mutagenesis assay (Ref. 383), the authors concluded that the combination of alkyl dimethyl amine oxide and alkyl dimethyl glycine inhibits the growth of microorganisms at some concentrations. Although small increases were observed in several strains of *S. typhimurium*, the authors stated that these increases were not reproducible and were attributed to random fluctuations that do not represent a mutagenic response to the test product. The test, therefore, has some limitations.

Eye and vagina¹ irritant tests have also been conducted. A 3-percent solution of alkyl dimethyl amine oxide and alkyl dimethyl glycine was judged to be a mild irritant in the eyes of dogs and a severe irritant in rabbits (Ref. 384). In an additional study conducted by a different institution, it was concluded that a 12.5-percent solution was not an irritant to rabbits. Results from vaginal irritation studies (Ref. 385) concluded that these ingredients produced an "acceptable" vaginal irritation score. However, it was unclear which concentrations were tested and what is an "acceptable" score. Six preparations appear to have been examined, but no information was presented on how they differed in composition.

The data also included a series of studies (Refs. 386, 387, and 388) evaluating a 10-percent solution of alkyl dimethyl amine oxide and alkyl dimethyl glycine as a body wash in nursing home patients. The evaluations appear to be largely subjective or gathered from interviews. Adverse effects were not observed.

Dentists gave the combination of these ingredients to subjects to use as a mouthrinse (Refs. 389 and 390). Overall adverse effects, including tingling, mucosal irritation, stain, and a peppery sensation on the tongue, were reported by 0.5 to 0.8 percent of users. Other dentists (Ref. 391) reported adverse effects in 1.3 percent of subjects.

The effects of the combination of these ingredients on mammalian cells were examined using a chromium release assay from human leukemic cells (H6-60). The release of chromium occurred at concentrations of 0.025 to 0.005 percent. As the report notes, "these findings are of some concern

since the effective window approximates the MIC for several bacterial species" (Ref. 392).

ii. *Effectiveness.* A number of studies have been carried out to assess the effects of this combination on the growth of oral bacteria and on the ability of oral microorganisms to produce acid from glucose.

The combination of alkyl dimethyl amine oxide and alkyl dimethyl glycine exhibits an antimicrobial effect against a wide range of microorganisms (Ref. 393). *Lactobacillus casei* is highly susceptible and is inhibited by as little as a 0.0004-percent solution. Several isolates of *Pseudomonas* are highly resistant to the combination. In general, the effect against gram-positive organisms was independent of pH. In contrast, the effect against gram-negative organisms was influenced by pH values. A 0.5-percent concentration of these ingredients completely inhibited bacterial glycolysis for 7 hours and inhibited the adherence of *S. sobrinus* to microtome wires. A lower concentration (0.05 percent) had less effect.

Twelve subjects (Ref. 394) rinsed with various concentrations of alkyl dimethyl amine oxide and alkyl dimethyl glycine and other preparations with only 2 days allowed between testing each material. Concentrations of 0.1 percent or higher reduced the population of total cultivable flora and total *Streptococcus* populations for at least 1 hour post rinse. Concentrations of 0.2 and 0.5 percent inhibited glycolysis in salivary sediment for several hours.

A clinical study involving 84 females and 42 males (aged 20 to 49) used a 0.25-percent solution (pH 6.8) of this combination (Ref. 395). Subjects were divided into one of three groups using a placebo, the test ingredients, or a positive control. Gender distribution was not disclosed. Following a complete prophylaxis, subjects rinsed twice daily for 6 weeks with 20 mL of solution. Subjects were instructed to continue their normal oral hygiene throughout the study. Plaque was assessed using Turesky modification of the Quigley-Hein Index. Mean plaque scores at the end of the study were as follows: Placebo, 2.53 ± 0.56 (2.44 ± 0.38), test ingredients, 2.05 ± 0.58 (2.45 ± 0.36), and positive control, 1.96 ± 0.33 (2.46 ± 0.31). An F test (test for equality of variances) comparison of the final three numbers showed statistical differences. An F test between the test solution and the positive control showed no statistically significant difference. No other statistical tests were reported. Gingivitis was not assessed.

A brief report (Ref. 396) claimed that a toothpaste containing these