

bicarbonate is safe, but appears to have relatively poor efficacy as an OTC antigingivitis/antiplaque agent, requiring high dosages and extended exposure time to have a reasonable chance at affecting the oral flora and clinical parameters.

Sodium bicarbonate has been used as an antacid as well as advocated as an ingredient in both toothpastes and mouthrinses. It has been generally regarded as a bactericidal agent that generates a hypertonic (causing water to flow out of the cell) environment, leading to disruption of the fluid equilibrium of the cell and dehydration, plasmolysis (cell shrinkage due to loss of water by osmosis), and eventual cell death.

i. *Safety.* Sodium bicarbonate is GRAS for use in foods (21 CFR 184.1736). Sodium bicarbonate is listed as an OTC antacid up to a maximum daily dose of 200 milliequivalent (mEq) bicarbonate ion (21 CFR 331.11(k)(1)). The usual dose is 1 to 5 g, providing up to 60 mEq. In OTC mouthrinse applications, sodium bicarbonate has been determined to be safe and effective for use as a debriding ingredient (47 FR 22712 at 22907, May 25, 1982). Ingestion of large amounts of sodium bicarbonate causes several blood chemistry changes, including increased sodium levels, resulting in toxic effects that produce hypernatremia (excessive amount of sodium in the blood) (Refs. 300, 301, and 302). The LD₅₀ is 7.57 to 8.9 g/kg body weight for the rat.

Sodium bicarbonate does not appear to be teratogenic or mutagenic using conventional testing, with no discernable effects on fetal survival in several species. It does not produce photosensitization, acute ocular irritation, or skin irritation by standard methods.

ii. *Effectiveness.* Few studies examine the effectiveness of sodium bicarbonate as a single active ingredient. Sodium bicarbonate has been found to be bactericidal to several oral microorganisms (Ref. 303). The authors suggest that the killing effect might be more than an osmotic imbalance created within the cells. This study showed several disturbing aspects about the effectiveness of this ingredient. For killing to be effective, relatively long periods of exposure were required, ranging from several minutes to hours. While a comparison to other antimicrobial agents is not intended as a criteria for effectiveness, sodium bicarbonate had a 10-fold poorer MIC range compared to sodium fluoride and a 1,000-fold poorer MIC range compared to sodium lauryl sulfate. In a study examining the effects of sodium

bicarbonate on *S. mutans*, osmotic disruption occurred through salt concentration dependent cell lysis (Ref. 304).

In a 20-day experiment on rats, sodium bicarbonate applications were ineffective at reducing plaque accumulations (Ref. 305). In a 6-week study comparing the effects of a toothpaste containing sodium bicarbonate with a standard fluoride toothpaste, no increase in effectiveness was observed (Ref. 306). In a similar 8-week study, no difference was observed in either plaque or gingivitis scores between the control and sodium bicarbonate test toothpaste (Ref. 307).

The Subcommittee concludes that sodium bicarbonate is safe, but there are insufficient data available to determine its effectiveness as an OTC antigingivitis/antiplaque agent.

f. *Sodium lauryl sulfate.* The Subcommittee concludes that sodium lauryl sulfate is safe at concentrations of 0.1 to 5 percent, but there is insufficient evidence to support its effectiveness as an antigingivitis/antiplaque active ingredient. The Subcommittee notes, however, that sodium lauryl sulfate is a safe and effective foaming ingredient in toothpaste.

Sodium lauryl sulfate is a synthetic detergent that acts as an anionic surfactant to lower surface tension. Sodium lauryl sulfate is available commercially as a viscous liquid, paste, or powder. It may contain small amounts of other sodium alkyl sulfates, although it consists mostly of sodium lauryl sulfate with a molecular weight of 288.4 and the formula CH₃(CH₂)₁₀CH₂OSO₃Na. It is soluble in water and alcohols. It binds to positively charged tooth surfaces and positively charged side groups of proteins. Protein binding may lead to denaturation (loss of biological activity) through conformational changes in the molecule. It is stable in alkaline solutions and will hydrolyze (split into fragments by addition of water) at room temperature below a pH of 5 (Ref. 308).

Sodium lauryl sulfate is used in cosmetics such as shampoos, deodorants, facial makeup, shaving preparations, and bath products, and in various oral care products. It is approved as a multipurpose food additive (21 CFR 172.822). Its ubiquity in personal care products can be estimated by a 1981 FDA Cosmetic Product Formulation List that shows it as an ingredient in 703 products (Ref. 308). In oral care products, sodium lauryl sulfate is used as a foaming agent and is frequently combined with other ingredients. It is found in mouthrinses and dentifrices, usually in

concentrations of 5 percent or less (Refs. 308 and 309). In most mouthrinses, it is found in concentrations of less than 1 percent. In skin care products, concentrations of sodium lauryl sulfate may range up to 50 percent. In the last two decades, sodium lauryl sulfate has replaced most other surfactants previously used for oral care drug products. It is estimated that 4 to 5 million pounds of sodium lauryl sulfate are used annually in the United States for oral health care products alone (Ref. 309).

The estimated daily intake of sodium lauryl sulfate of about 1 to 10 mg originates, in part, from personal products (including oral hygiene products), foods, and drinking water. Personal products account for about one-half or less of this intake (Ref. 310).

i. *Safety.* Extensive safety data, both in animals and humans, show that sodium lauryl sulfate has a very low level of toxicity at doses used in oral health care products, is rapidly metabolized through the liver, and has no genotoxic or teratogenic effects (Ref. 311).

1. *Absorption and excretion.* Sodium lauryl sulfate is poorly absorbed through the epithelial lining of the skin and mucosal surfaces. Aqueous radio-labeled sodium lauryl sulfate was applied to guinea pig skin in vivo by rubbing for 10 minutes, followed by washing and application of a nonocclusive dressing for 24 hours (Ref. 308). Most of the radioactivity was recovered on the skin at the experimental site, in the washing fluid, and in the dressing. Radioactivity of 0.1 percent was recovered from exhaled air and urine. No radioactivity was found in the internal organs, feces, or carcass. The studies concluded that the presence of a strong anionic terminal group impaired sodium lauryl sulfate penetration through the skin.

Rat skin was exposed for 15 minutes to radio-labeled (25 millimolar (mM)) sodium lauryl sulfate. Expired carbon dioxide, urine, feces, and skin were monitored for 24 hours. Autoradiography showed heavy concentrations of sodium lauryl sulfate on the skin surface and in the hair follicles. Quantifiable levels of sodium lauryl sulfate were also recovered in the urine (Ref. 308).

If linear alkyl sulfates, including sodium lauryl sulfate, are deposited on the skin after a wash and rinse application, only a small amount actually penetrates the skin (Refs. 312 and 313). Sodium lauryl sulfate is rapidly absorbed through the intestine of mammals, rapidly metabolized through the liver, and is excreted in the