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Final Report on the Safety Assessment of Sodium Sesquicarbonate, Sodium Bicarbonate, and Sodium Carbonate

Sodium Sesquicarbonate, Sodium Carbonate, and Sodium Bicarbonate are used in cosmetic products at concentrations ranging up to 50%. The LD_{50} in rats for Sodium Bicarbonate ranged from 7.6 g/kg to 8.9 g/kg. Sodium Sesquicarbonate, Sodium Carbonate, and Sodium Bicarbonate caused conjunctivitis. Sodium Bicarbonate was not an ocular irritant to laboratory animals. Neither Sodium Bicarbonate nor Sodium Carbonate was a teratogen to laboratory animals. Sodium Sesquicarbonate and Sodium Bicarbonate were not mutagenic to two different cell cultures. Dermatitis, but not sensitization, was observed in employees of a Trona (Sodium Sesquicarbonate) mining facility. Sodium Carbonate, but not Sodium Bicarbonate, is a skin and eye irritant due to the alkaline nature of its solutions. The cosmetic use of Sodium Carbonate at high concentrations is mainly limited to products designed to be diluted before use and in products where pH is buffered to near neutrality. It is concluded that Sodium Sesquicarbonate, Sodium Bicarbonate, and Sodium Carbonate are safe as presently used in cosmetics.

CHEMISTRY

Sodium Sesquicarbonate is composed of Sodium Carbonate and Sodium Bicarbonate. Hence, the three sodium compounds are addressed in this report.* Physical properties of these compounds are listed in Table 1.

*This report updates studies of Sodium Sesquicarbonate, Sodium Bicarbonate, and Sodium Carbonate included in a 1975 GRAS report entitled *Evaluation of the Health Aspects of Carbonates and Bicarbonates as Food Ingredients.*

TABLE 1. Properties of Sodium Compounds[6]

	Sodium Sesquicarbonate	*Sodium Carbonate*	*Sodium Bicarbonate*
Formula	$Na_2CO_3 \cdot NaHCO_3 \cdot 2H_2O$	Na_2CO_3	$NaHCO_3$
Molecular weight	226.03	105.99	84.00
Crystalline form	Colorless, monoclinic	White, hygroscopic powder	White, monoclinic prisms
Boiling Point	– – –	Decomposes	– – –
Melting point	Decomposes	851°C	270°C
Density	2.112	2.532	2.159
Refractive index	1.5073	1.535	1.500
Solubility	Soluble in water	Soluble in water, slightly soluble in absolute alcohol, and insoluble in acetone	Soluble in water, slightly soluble in alcohol

Definition and Properties

Sodium Sesquicarbonate

Sodium Sesquicarbonate (CAS No. 533-96-0) is a white crystalline solid in either flake or powder form, known also as trona and urao.[1,2] It dissolves rapidly and completely in water, and its solutions are alkaline (0.1 M aqueous solution, pH 10.1).[1,3]

Sodium Carbonate

Sodium Carbonate (CAS Nos. 497-19-8 and 5968-11-6), known as soda ash and carbonic acid, disodium salt,[4] is a grayish white crystalline powder.[5] It is soluble in water and its aqueous solution is strongly alkaline (0.1 M, pH = 11.6).[2]

Sodium Bicarbonate

Sodium Bicarbonate (CAS No. 144-55-8) is a white crystalline solid in either powder or granule form.[2] Synonyms for this compound include baking soda, bicarbonate of soda, carbonic acid, monosodium salt.[4] The decomposition of Sodium Bicarbonate to Sodium Carbonate and carbon dioxide in aqueous solution is initiated at approximately 20°C; boiling completes the decomposition process.[2] A freshly prepared 0.1 M aqueous solution of Sodium Bicarbonate has a pH of 8.5.[2]

Methods of Production

Sodium Sesquicarbonate

Sodium Sesquicarbonate occurs naturally as trona ore and is produced via a double refining process; it is also prepared by partial carbonation of a soda ash solution, followed by crystallization, centrifugation, and drying.[7] The soda ash solution undergoing crystallization contains equimolar quantities of Sodium Car-

bonate and Sodium Bicarbonate.[5] Sodium Sesquicarbonate has been widely produced from Sodium Carbonate and a slight excess of Sodium Bicarbonate.[8]

Sodium Carbonate and Sodium Bicarbonate

Sodium Carbonate and Sodium Bicarbonate may be produced by the Solvay process.[9,10] In this process, carbon dioxide is bubbled through a solution of sodium chloride and ammonia to precipitate Sodium Bicarbonate; calcination of the Sodium Bicarbonate produces Sodium Carbonate.

Reactivity

X-ray diffraction patterns of Sodium Sesquicarbonate (trona), Sodium Bicarbonate, and Sodium Carbonate exposed to sulfur dioxide (SO_2) at 271°C indicate: the complete reaction of trona to sodium pyrosulfite and one form of sodium sulfate, the complete reaction of Sodium bicarbonate to sodium pyrosulfite, and no sulfur-bearing phases for the Sodium Carbonate sample.[11]

Analytical Methods

X-ray diffraction and scanning electron microscopy (in conjunction with energy dispersive x-ray analysis) are methods by which Sodium Sesquicarbonate, Sodium Carbonate, and Sodium Bicarbonate have been identified.[11]

Impurities

Sodium Sesquicarbonate

Results from assays of Sodium Sesquicarbonate indicate the presence of Sodium Bicarbonate (not less than 35.0% and not greater than 38.6%) and Sodium Carbonate (not less than 46.4% and not greater than 50.0%).[1] The following impurities have also been reported:

	FASEB[12]	*Food Chemicals Codex*[1]	*Estrin et al.*[13]
Arsenic	3 ppm[a]	3.000 ppm[a]	3 ppm maximum
Lead	10 ppm[a]	10.000 ppm[a]	20 ppm maximum
Iron	20 ppm[a]	0.002%	20 ppm maximum
Sodium chloride	5000 ppm[a]	0.500%	– – –
Water	– – –	13.8–16.7%	– – –

[a]Not greater than.

Sodium Carbonate

Sodium Carbonate consists of not less than 99.5% Sodium Carbonate, calculated on the anhydrous basis.[14] The Cosmetic, Toiletry and Fragrance Association (CTFA) specification for Sodium Carbonate lists arsenic (3 ppm maximum) and lead (20 ppm maximum) as impurities.[13] Other impurities include sodium chloride, sodium sulfate, calcium carbonate, magnesium carbonate, and Sodium Bicarbonate.[5]

Sodium Bicarbonate

Sodium Bicarbonate consists of not less than 99.0% Sodium Bicarbonate, calculated on the dried basis.[15] High purity commercial grades contain approximately 27.3% sodium.[16]

USE

Purpose in Cosmetics

Sodium Sesquicarbonate serves as a water softener in bath preparations.[17] Product formulation data[18] indicate that Sodium Sesquicarbonate occurs predominantly in bath preparations, whereas Sodium Bicarbonate and Sodium Carbonate (components of Sodium Sesquicarbonate) are used in bath, skin, and hair preparations.

The cosmetic formulation listing that is made available by the Food and Drug Administration (FDA) is compiled through voluntary filing of such data in accordance with Title 21 part 720.4 of the Code of Federal Regulations.[7] Ingredients are listed in prescribed concentration ranges under specific product type categories. Since certain cosmetic ingredients are supplied by the manufacturer at less than 100% concentration, the value reported by the cosmetic formulator may not necessarily reflect the actual concentration found in the finished product; the actual concentration in such a case would be a fraction of that reported to the FDA. The fact that data are only submitted within the framework of preset concentration ranges also provides the opportunity for overestimation of the actual concentration of an ingredient in a particular product. An entry at the lowest end of a concentration range is considered the same as one entered at the highest end of that range, thus introducing the possibility of a two- to ten-fold error in the assumed ingredient concentration. The product formulation listings for Sodium Sesquicarbonate, Sodium Carbonate, and Sodium Bicarbonate are shown in Table 2. Sodium Sesquicarbonate occurs predominantly in bath preparations, ranging in concentration from >1–5% to >50%. Sodium Carbonate and Sodium Bicarbonate are found mostly in bath, skin, and hair preparations. Sodium Carbonate ranges in concentration from ≤ 0.1% to >10–25% and Sodium Bicarbonate from ≤ 0.1% to >50% in these preparations.

Surfaces to which Applied

Cosmetic products containing Sodium Sesquicarbonate, Sodium Carbonate, and Sodium Bicarbonate are applied to the skin and hair and may come in contact with the eyes, nasal mucosa, and other parts of the body.

Frequency and Duration of Application

Product formulations containing Sodium Sesquicarbonate, Sodium Carbonate, and Sodium Bicarbonate may be applied on a monthly basis or as often as several times daily. Many of the products may be expected to remain in contact with the skin for an hour at most and may be used repeatedly over a period of several years.

High concentrations of Sodium Carbonate and Sodium Bicarbonate occur mostly in bath formulations. In-use studies have indicated that approximately 17.0 g of any bubble bath formulation are diluted with approximately 15 gallons of water. Thus, the final concentration of bubble bath would be approximately 0.03%. For bath preparations in which Sodium Bicarbonate or Sodium Carbonate is present at concentrations of 25 or 50%, consumer exposure would amount to 0.0075 or 0.015%, respectively.[19]

Noncosmetic use

The Select Committee on Generally Recognized as Safe (GRAS) Substances (1975) concluded that there were no reasonable grounds for suspecting any hazards associated with using Sodium Sesquicarbonate, Sodium Carbonate, and Sodium Bicarbonate as food ingredients.[12] The conclusion was based on data from the following types of studies: acute studies,[20-23] subchronic and chronic feeding studies,[24] other feeding studies,[25-28] metabolic studies,[29-36] teratogenicity studies,[37,38] mutagenicity studies,[39] and clinical studies concerning digestion,[40] metabolism,[41,42] absorption and excretion,[43] urinary excretion,[44] renal function,[45] acid–base balance and renal function,[46-48] and exercise physiology.[49] Currently, Sodium Sesquicarbonate, Sodium Carbonate, and Sodium Bicarbonate are GRAS direct human food ingredients, with no limitations other than current good manufacturing practices.[7]

Sodium Sesquicarbonate is not included in the 1984 Over-The-Counter (OTC) Drug Review, but its major components, Sodium Carbonate and Sodium Bicarbonate, are listed as antacids that are GRAS.[50]

In addition to their use in food and pharmaceutical products, Sodium Sesquicarbonate, Sodium Carbonate, and Sodium Bicarbonate are used in aluminum production, textile processing, petroleum refining, and in the manufacture of soap, glass, and paper.[5,51]

BIOLOGICAL PROPERTIES

Absorption, Metabolism, and Excretion

The major extracellular buffer in the blood and interstitial fluid of vertebrates is the bicarbonate buffer system, described by the following equation:

$$H_2O + CO_2 \rightleftharpoons H_2CO_3 \leftrightharpoons H^+ + HCO_3^-$$

Carbon dioxide from the tissues diffuses rapidly into red blood cells, where it is hydrated with water to form carbonic acid. This reaction is accelerated by carbonic anhydrase, an enzyme present in high concentrations in red blood cells. The carbonic acid formed dissociates into bicarbonate and hydrogen ions. Most of the bicarbonate ions diffuse into the plasma. Since the ratio of H_2CO_3 to dissolved CO_2 is constant at equilibrium, pH may be expressed in terms of bicarbonate ion concentration and partial pressure of CO_2 by means of the Henderson-Hasselbach equation:

$$pH = pk' + \log [HCO_3^-]/\alpha P_{CO_2}$$

TABLE 2. Product Formulation Data[18]

Product category	Total no. of formulations in category	Total no. containing ingredient	No. of product formulations within each concentration range (%)						
			>50	>25–50	>10–25	>5–10	>1–5	>0.1–1	≤0.1
Sodium Sesquicarbonate									
Bath oils, tablets, and salts	237	24	5	7	6	4	2	–	–
Bubble baths	475	68	39	19	4	6	–	–	–
Bath capsules	3	2	–	–	2	–	–	–	–
Other bath preparations	132	11	–	2	6	3	–	–	–
Other fragrance preparations	191	1	–	–	–	1	–	–	–
Hair straighteners	64	1	1	–	–	–	–	–	–
Permanent waves	474	2	–	–	–	1	1	–	–
Other personal cleanliness products	227	2	–	–	–	2	–	–	–
1981 TOTALS		111	45	28	18	17	3	–	–
Sodium Carbonate									
Bubble baths	475	4	–	–	4	–	–	–	–
Hair conditioners	478	1	–	–	–	–	–	1	–
Hair straighteners	64	1	–	–	–	–	1	–	–
Permanent waves	474	1	–	–	–	–	1	–	–
Hair shampoos (noncoloring)	909	2	–	–	–	–	–	1	1
Hair dyes and colors (all types requiring caution statement and patch test)	811	1	–	–	–	–	1	–	–
Hair bleaches	111	2	–	–	–	1	–	1	–
Makeup foundations	740	1	–	–	–	–	–	–	1
Bath soaps and detergents	148	2	–	–	–	–	–	2	–
Douches	26	1	–	–	–	1	–	–	–
Other personal cleanliness products	227	3	–	–	–	–	2	–	1

Skin cleansing preparations (cold creams, lotions, liquids, and pads)	680	2	–	–	–	–	–	–	2
Hormone skin care preparations	10	1	–	–	–	–	–	–	1
Moisturizing skin care preparations	747	2	–	–	–	–	–	–	2
Skin fresheners	260	1	–	–	–	–	–	–	1
1981 TOTALS		25	–	–	4	2	5	5	9
Sodium Bicarbonate									
Bath oils, tablets, and salts	237	1	–	–	–	–	1	–	–
Bubble baths	475	4	–	–	4	–	–	–	–
Eyeliner	396	2	–	–	–	–	–	1	1
Fragrance powders (dusting and talcum, excluding aftershave talc)	483	5	–	–	4	–	–	1	–
Hair straighteners	64	1	–	–	–	–	–	1	–
Permanent waves	474	5	–	–	–	–	–	3	2
Other hair preparations (noncoloring)	177	1	–	–	–	–	1	–	–
Hair bleaches	111	1	–	1	–	–	–	–	–
Dentifrices (aerosol, liquid, pastes, and powders)	42	5	1	2	–	1	1	–	–
Deodorants (underarm)	239	2	–	–	–	–	2	–	–
Douches	26	4	–	–	1	–	1	1	1
Other personal cleanliness products	227	4	–	–	1	1	–	–	2
Other shaving preparation products	29	1	–	–	–	–	–	–	1
Paste masks (mud packs)	171	3	1	–	–	–	–	–	2
Skin fresheners	260	2	–	–	–	1	–	–	1
Other skin care preparations	349	4	–	–	4	–	–	–	–
1981 TOTALS		45	2	3	14	3	6	7	10

The blood plasma of man normally has a pH of 7.40. Should the pH fall below 7.0 or rise above 7.8, irreparable damage may occur. Compensatory mechanisms for acid–base disturbances function to alter the ratio of HCO_3^- to P_{CO_2}, returning the pH of the blood to normal. Thus, metabolic acidosis may be compensated for by hyperventilation and increased renal reabsorption of HCO_3^-. Metabolic alkalosis may be compensated for by hypoventilation and the excretion of excess HCO_3^- in the urine.[52–54]

^{14}C-Sodium Bicarbonate (18 μCi) was introduced via intraperitoneal injection into CFW mice.[35] Subsequently, assays of the blood and various organs of the body were performed (after 24 and 48 h and 1, 2, 4, and 12 weeks). After 1 h, more than 90% of the total radioactivity injected was lost through the lungs. Most of the radioactivity in the blood was in noncarbonate form after 24 h. In another study, five intraperitoneal injections of Sodium [^{11}C] Bicarbonate (made at 30-minute intervals) were administered to rats that had been fasted for 24 h.[33] The animals were killed 30 minutes after the last injection, and about 60% of the radioactivity was accounted for. The urine contained 1.3% of the radioactivity, and more than 50% of the radioactivity appeared as respiratory [^{11}C] carbon dioxide.

In humans, when plasma bicarbonate concentrations are below 24 mM, nearly all of the bicarbonate entering the renal tubules is reabsorbed; above this plasma level, excess bicarbonate is excreted.[47]

TOXICOLOGY

Inhalation Toxicity

Male rats were subjected to a Sodium Carbonate aerosol over a period of 3½ months.[55] The aerosol consisted of a 2% aqueous solution of Sodium Carbonate and the frequency of exposure was 4 h per day for 5 days per week. Pulmonary alterations included thickening of the intraalveolar walls, hyperemia, lymphoid infiltration, and pneumocyte desquamation (aerosol concentration = 70 ± 2.9 mg/m^3).

In another study, adult male rats (10, Sprague-Dawley and Wistar strains), mice (20, Swiss-Webster strain), and guinea pigs (10, Hartley-albino strain), were exposed to aerosols, consisting predominantly of Sodium Carbonate, for a period of 2 h.[56] Exposures occurred in a chamber described by Zwicker et al.[57] and at the following aerosol concentration ranges: 800–4600 mg/m^3 (rats), 600–3000 mg/m^3 (mice), and 500–3000 mg/m^3 (guinea pigs). For all aerosol concentration ranges, rats, mice, and guinea pigs had signs of respiratory impairment immediately after exposure. Clinical signs included dyspnea, wheezing, excessive salivation, and distention of the abdomen. Most of the deaths occurred during two periods: (1) during exposure and within 1–2 h afterward or (2) beginning at 1 day after exposure, peaking at 5–7 days, and continuing to 9–10 days after exposure. Some animals died less than 1 h after the beginning of exposure. The number of animals that died at various intervals during exposures was not given. Lesions in animals that died during or shortly after exposure were present in the posterior pharynx, larynx, anterior trachea, and, in approximately 3% of the animals, the lungs. For animals that survived for 1–14 days, lesions in the respiratory tract were limited to the laryngeal mucosa.

Acute Oral Toxicity

Sodium Bicarbonate was given to Wistar SPF rats (weighing 100–150 g) via stomach tube.[23] The LD_{50} values reported were 8.9 g/kg (fed rats), 7.57 g/kg (fasted rats on wire floored cages), and 8.46 g/kg (fasted rats bedded on wood shavings).

Ten adult white rats (fasted for 24 h) were given 5 g/kg of Sodium Bicarbonate via gavage. One animal died 6 h after administration. The test substance did not induce toxic effects in the remaining nine rats.[58]

Ten CFE rats of the Carworth strain (weight range 200–300 g) were given 5 g/kg of Sodium Bicarbonate via gastric intubation. Each single administration was followed by a 14-day observation period. One death was reported. Sodium Bicarbonate was not classified as a toxic substance, since one half or more of the test animals did not die.[59]

Subchronic Oral Toxicity

Ten White Leghorn chicks (15 days old) were given 0.5% Sodium Bicarbonate in drinking water for 75 days.[60] The 10 control chicks received unsupplemented feed and water. Blood samples from both groups were drawn every 15 days, and pooled samples were used for biochemical analyses. A gradual rise in total protein (TP), uric aicd (UA), and nonprotein nitrogen (NPN) in the serum was reported for Sodium Bicarbonate-fed chicks. The increase in TP was statistically significant on the 45th day of feeding, whereas UA and NPN increased significantly on the 15th day. The authors noted excessive watery droppings following Sodium Bicarbonate administration as the possible cause of dehydration and the concentration of serum proteins. Significantly high UA values were attributed possibly to nephrotoxic effects of Sodium Bicarbonate, which led to decreased excretion of UA. Significantly high NPN values were attributed to hyperuric acidemia.

Ocular Irritation

A survey of ocular irritation studies indicated that alkalis generally were injurious to the corneal stroma, regardless of the type, as long as the pH was greater than 12.0.[61]

The potential for various alkalies to cause ocular irritation was evaluated in New Zealand albino rabbits (male and female) weighing 2.0–2.5 kg; two groups of at least six rabbits each were used for each material tested.[62] Sodium Carbonate, Sodium Sesquicarbonate, and Sodium Bicarbonate were administered in powder form (0.1 ml) to the central portion of the cornea of the right eye. The left eye served as the untreated control. The eyes of the first group of rabbits were rinsed for 2 minutes with 300 ml of tap water 30 seconds after exposure (rinsed eyes); the eyes tested in the second group were not rinsed after exposure (unrinsed eyes). Control and treated eyes were scored at 1 h and days 1, 2, 3, and 7 after exposure according to the scale of Draize et al.[63]: corneal opacity (0–4), iritis (0–10). Treated eyes of both groups were stained with fluorescein 1 h after the initial exposure and subsequently examined grossly for any damage to the cornea, iris, or conjunctiva. The concentrations and pH values of the alkalies tested and the number of rabbits with corneal opacities in the rinsed and un-

rinsed groups are shown in Table 3. Corneal opacities were produced in unrinsed eyes within 1 h after exposure to Sodium Carbonate, and the severest effect was noted by day 3 (mean Draize intensity score = 3.8 ± 0.2); the severity was maintained through day 7. In rinsed eyes, corneal opacities were observed on day 2 (mean Draize intensity score = 0.8 ± 0.5) and had disappeared by day 7. Iritis was observed in unrinsed eyes at 1 h after exposure to Sodium Carbonate, and a mean Draize score of 2.0 ± 0.0 was reported on days 1, 2, 3, and 7; in rinsed eyes, iritis was noted at 1 h after exposure and had disappeared by day 3. The incidence of iritis is as listed in Table 3 for corneal opacities. Sodium Carbonate also produced pannus in 3/6 unrinsed and 4/6 rinsed eyes, and keratoconus in 2/12 unrinsed eyes. Sodium Carbonate, Sodium Sesquicarbonate, and Sodium Bicarbonate produced conjunctivitis, which persisted through day 7 in all animals tested.

In another study, the ocular irritation potential of Sodium Bicarbonate was determined using six albino rabbits. The test substance (0.086 g) was instilled into the right eye of each animal; the left eye served as the untreated control. Treated and control eyes were examined every 24 h for a period of 3 days. Ocular irritation was scored according to the scale by Draize.[64] The results were as follows: one animal had slight conjunctival redness at 48 h postinstillation, three animals had slight conjunctival redness at 48 and 72 h, and two animals had slight conjunctival redness at 24, 48, and 72 h (one of the two animals also had slight conjunctival chemosis and discharge at 24 h). It was concluded that the test substance could not be classified as an ocular irritant.[65]

One-tenth milliliter of Sodium Bicarbonate was instilled into one eye (conjunctival sac) of each of six albino rabbits. Observations for signs of irritation were made during 1 week after instillation. The test substance did not induce ocular irritation in any of the rabbits.[58]

Skin Irritation

Contact of alkaline materials with the skin may cause irritation, corrosion, or erosion. Such materials react with tissue proteins to form albuminates and gelatinized tissues, resulting in deep injuries.[10]

TABLE 3. Corneal Opacities in Rinsed and Unrinsed Rabbit Eyes after Exposure to Alkalies at Different Concentration and pHs[62]

Alkali	*Concentration % w/v*	*No. of animals with corneal opacities*[a]		
		pH	*Rinsed*[b]	*Unrinsed*
Sodium Carbonate (anhydrous)	100.0	11.3[c]	2/6	12/12
Sodium Sesquicarbonate	100.0	9.9[c]	0/6	0/6
Sodium Bicarbonate	100.0	8.3[c]	0/6	0/6

[a]Number of animals out of number tested that exhibited the response.
[b]Tested eyes were irrigated with water for 2 minutes following a 30-second residence of the alkali.
[c]pH obtained from saturated solutions.

An aqueous solution of Sodium Carbonate (50% w/v) was placed on the skins (intact and abraded) of rabbits and guinea pigs.[66] The animals were examined at 4, 24, and 48 h after application of the solution for erythema, edema, and corrosion. The abraded skins of the rabbits had moderate erythema and edema, and those of the guinea pigs were negligibly affected. There were no signs of erythema, edema, or corrosion in the intact skins.

Sodium Bicarbonate (0.5 g) was applied to the abraded and nonabraded skin of six rabbits by means of patches made of surgical gauze. The patches remained in contact with the skin for 24 h. Examinations for signs of irritation were made immediately after patch removal and 48 and 72 h thereafter. None of the animals had signs of skin irritation.[58]

The skin irritation potential of Sodium Bicarbonate was determined using six albino rabbits. The test substance (0.5 g) was applied to both abraded and nonabraded clipped skin of the back of each animal via occlusive patches. Observations for signs of irritation were made at the end of the 24-h contact period and 48 h later. It was concluded that the test substance was not a primary irritant.[67]

Teratogenicity

Aqueous solutions of Sodium Carbonate were administered via oral intubation to pregnant mice at doses ranging from 3.4 to 340 mg/kg during days 6–15 of gestation. The test substance did not affect implantation or hinder the survival of dams or fetuses. Soft and skeletal tissue anomalies were noted in the experimental group, but the incidence of these findings did not differ from that of sham-treated controls. Similar negative results were reported for rats and rabbits at doses of 245 mg/kg and 179 mg/kg, respectively.[68]

Sodium Bicarbonate did not induce teratogenic effects when administered orally at the following doses: 580 mg/kg (mice), 340 mg/kg (rats), and 330 mg/kg (rabbits).[69]

Mutagenicity

The mutagenic potential of Sodium Sesquicarbonate was evaluated by means of the spot test and the plate incorporation test according to the methods of Ames et al.[70] The tests were conducted with mutant strains TA98, TA100, TA1535, TA1537, and TA1538 of *Salmonella typhimurium* LT2. In the spot test, Sodium Sesquicarbonate was mutagenic to strain TA100. Sodium Sesquicarbonate was not mutagenic to any of the strains examined in the plate incorporation test, having caused no statistically significant increases in the number of revertant colonies over that of solvent controls in either the presence or absence of metabolic activation.[71]

Sodium Bicarbonate was not mutagenic to *Saccharomyces cerevisiae* strain D4 and *Salmonella typhimurium* strains TA1535, TA1537, and TA1538 in suspension and plate tests, both in the presence and absence of metabolic activation.[39]

CLINICAL ASSESSMENT OF SAFETY

Skin and Mucous Membrane Irritation

Two hundred thirty employees (miners and surface workers) at a trona ore mining facility participated in a clinical study. Their mean age was 37.6, and the mean working period was 10.0 years. "Trona dermatitis" was detected in 115 of the employees and was characterized by pruritic, erythematous, raised, dry, and fissured lesions, commonly affecting the hands, arms, and legs. Dermatitis was uncommon among subjects before they began Trona mining. Fifty-eight (25%) of the 230 examined workers showed signs of mucous membrane inflammation, including 23 and 26 with conjunctivitis and pharyngeal inflammation, respectively. Ulcerations of the nasal or oral mucosa were noted in 4 workers. Employees showing signs of mucous membrane inflammation or ulceration were among the 115 with trona dermatitis. Sixty-seven of the 115 workers were selected for patch testing. Finn chambers were placed on the outer aspect of the arm and removed after 48 h. Test results were negative for 10% aqueous Sodium Carbonate and 10% aqueous raw trona. These results indicated that trona ore was an irritant but not a sensitizer.[72]

Skin Irritation and Sensitization

A bar soap product containing 0.25% Sodium Carbonate was evaluated for its skin irritation and sensitization potential at a concentration of 1% in water (effective Na_2CO_3 concentration = 0.0025%). The procedure was a modification of the Draize test for human sensitization.[64] Two-tenths milliliter of the test substance was applied to the back of each of 109 male and female subjects (>17 years old) via occlusive patches. During the induction phase, the first patch remained for 24 h and the site was then scored according to the scale by Draize.[64]: erythema (0–4). The next patch was applied 24 h after scoring. This procedure was repeated for a total of 10 induction exposures. The first challenge patch remained for 24 h and the site was then scored. Following a 24 h nontreatment period, a second challenge patch was applied and remained for 24 h. Grading occurred immediately after removal of the patch and 48 h later. Two subjects had very slight erythema and two had well-defined erythema during induction. At the end of the first challenge, four subjects had very slight erythema and one had well-defined erythema. Two subjects had well-defined erythema at the end of the second challenge. Very slight and well-defined erythema were observed in three subjects and one subject, respectively, 48 h after removal of the second challenge patch. The reactions observed were indicative of the weak, nonspecific irritation seen when occlusive patch testing of soap products is conducted. It was concluded that the soap product was neither a strong irritant nor a contact sensitizer.[73] In a similar study, Sodium Carbonate was tested at the same concentration (0.0025%) in another bar soap product. Occlusive patches were applied to 109 male and female subjects (>17 years old) according to the protocol previously mentioned. Four and three subjects had very slight and well-defined erythema, respectively, during induction. At the end of the first challenge, three and two subjects had very slight and well-defined erythema, respectively. Three subjects had well-defined erythema at the end of the second

challenge. Very slight and well-defined erythema were observed in one and two subjects, respectively, 48 h after removal of the second challenge patch. It was concluded that the soap product was neither a strong irritant nor a contact sensitizer.[74] In another study (same protocol) involving 107 male and female subjects (>17 years old), Sodium Carbonate was again tested at a concentration of 0.0025% in a different bar soap product. The grading scale for irritation ranged from 1 (mild erythema) to 4 (intense erythema with edema and vesicles). Three and two subjects had mild and intense erythema, respectively, during induction. At the end of the first challenge, mild erythema was observed in one subject and intense erythema in another. Mild and intense erythema were observed in two subjects and one subject, respectively, after the second challenge. It was concluded that the soap product was neither a strong irritant nor an allergen.[75]

The skin irritation and sensitization potential of a bar soap product containing 0.25% Sodium Carbonate was evaluated with 41 male and female subjects (>17 years old) according to a modified Draize test for human sensitization. Two-tenths milliliter of the product was applied via occlusive patches (24-h exposure) at a concentration of 1% in water (effective Na_2CO_3 concentration = 0.0025%). Induction applications, separated by a 24 h nontreatment period, were made to the arm three times per week for a period of 3 weeks. Irritation was scored immediately after the 24-h exposure according to the scale: 0–4 (intense erythema, edema, and vesicles). Challenge sites were graded immediately after the 24-h exposure and 72 h later. The number of subjects with mild erythema ranged from 15 (third insult) to 23 (ninth insult). One subject had mild erythema 24 h after application of the challenge patch. It was concluded that the product was neither a strong irritant nor a sensitizer.[76] In a similar study (same protocol), 0.2 ml of another bar soap product containing 0.25% Sodium Carbonate was tested at a concentration of 1% in water. Forty-one male and female subjects participated in the study. Observations of mild erythema ranged from 1 subject (second insult) to 18 subjects (ninth insult). The number of subjects with intense erythema ranged from 1 (third insult) to 12 (ninth insult). Four and three subjects had mild erythema at the original site 24 and 96 h after application of the challenge patch, respectively. Four subjects and one subject had mild erythema at an alternate site 24 and 96 h after application of the challenge patch, respectively. One subject had intense erythema at the original site 24 h after application of the challenge patch. It was concluded that the product was neither a strong irritant nor a sensitizer.[77] The same conclusion was stated in two other studies (same protocol) in which 53 subjects were patch tested (occlusive patches) with bar soap products containing 0.25% Sodium Carbonate at a concentration of 1% in water.[78,79]

Case Reports

Reports in which baking soda (Sodium Bicarbonate) was administered to children as a home remedy for various symptoms are available.[80–82] Symptoms consistent with alkalosis and impaired renal function were present. A diffuse erythematous rash with large areas of denuded skin was also observed when baking soda was applied directly to the skin.

SUMMARY

Sodium Sesquicarbonate, Sodium Carbonate, and Sodium Bicarbonate are inorganic crystalline compounds. In cosmetic products, they are used predominantly in bath, hair, and skin preparations. Noncosmetic uses include aluminum production, textile processing, petroleum refining, and the manufacture of soap, glass, and paper.

The inhalation of aerosols containing Sodium Carbonate has resulted in pathological changes within the lungs and respiratory passages of mice, rats, and guinea pigs.

In an acute oral toxicity study of Sodium Bicarbonate, LD_{50} values were 7.57 g/kg and 8.9 g/kg in fasted and fed rats, respectively. Sodium Bicarbonate was classified as a nontoxic substance in another acute oral study. Nephrotoxic effects were associated with the subchronic oral administration of Sodium Bicarbonate to white Leghorn chicks.

In an ocular irritation study involving rabbits, applications of Sodium Sesquicarbonate, Sodium Carbonate, and Sodium Bicarbonate caused conjunctivitis. Results from other ocular iritation studies indicated that Sodium Bicarbonate was not an ocular irritant in albino rabbits.

The application of an aqueous solution of Sodium Carbonate to intact and abraded skins of rabbits and guinea pigs produced irritation only in abraded skin. Sodium Bicarbonate did not cause irritation when applied to abraded and nonabraded skins of rabbits.

No teratogenic effects were noted when Sodium Bicarbonate and Sodium Carbonate were administered to pregnasnt rats, mice, and rabbits.

Sodium Sesquicarbonate was not mutagenic in *Salmonella typhimurium* LT2 mutant strains in the plate incorporation test but was mutagenic to strain TA100 in the spot test. Sodium Bicarbonate was not mutagenic to *Saccharomyces cerevisiae* and *Salmonella typhimurium* mutant strains in both suspension and plate tests.

Dermatitis, but not sensitization, was observed in employees of a trona (Sodium Sesquicarbonate) mining facility. The dermal application of Sodium Bicarbonate has been associated with the development of a rash and metabolic alkalosis in infants. Results from human skin irritation and sensitization studies indicated that a soap product containing 0.25% Sodium Carbonate was neither a strong irritant nor a sensitizer.

DISCUSSION

Sodium Carbonate, but not Sodium Bicarbonate, is a skin and eye irritant due to the alkaline nature of its solutions. Highly concentrated solutions of Sodium Carbonate have a pH of greater than 11. The cosmetic use of Sodium Carbonate at high concentrations is mainly limited to products designed to be diluted before use and in products where pH is buffered to near neutrality.

The available data on human skin sensitization are limited to the occupational testing of workers exposed to high levels of Sodium Sesquicarbonate and the testing of formulations containing low concentrations of Sodium Carbonate. A review of the combined data from sensitization studies indicates that neither

Sodium Carbonate nor Sodium Sesquicarbonate is a human sensitizer. Phototoxicity data are not available. However, the Panel notes the lack of a chromophore in these cosmetic ingredients and does not consider that testing for phototoxicity is warranted.

CONCLUSION

Based on the available data, Sodium Sesquicarbonate, Sodium Bicarbonate, and Sodium Carbonate are safe as presently used in cosmetics.

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