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Final Report on the Safety Assessment of Polyquaternium-10

Polyquaternium-10 is a polymeric quaternary ammonium derivative of hydroxyethyl cellulose that is used in cosmetics as a conditioner, thickener, and emollient at concentrations of ≤0.1%–5%. Polyquaternium-10 has, at most, only a low potential to penetrate the stratum corneum but is adsorbed by keratinous surfaces. The oral LD_{50} of Polyquaternium-10 was not obtained at 16 g/kg in rats. Inhalation, dermal, and ocular animal test data indicated, at most, only a low degree of toxicity at test concentrations of Polyquaternium-10 greater than that used in cosmetic products. Polyquaternium-10 with and without metabolic activation was not a mutagen in three separate assay systems. Polyquaternium-10 was neither an irritant nor a human sensitizer when tested at 2.0%. Cosmetic products containing up to 1% Polyquaternium-10 were not human irritants, sensitizers, or photosensitizers. On the basis of the information presented, it is concluded that Polyquaternium-10 is safe as a cosmetic ingredient in the present practices of use.

INTRODUCTION

Polyquaternium-10 is a cationic form of hydroxyethyl cellulose that adsorbs and sorbs well to proteinaceous surfaces. It is used in cosmetics as a conditioner, thickener, and emollient in hair care products, lotions, and makeup.

CHEMISTRY

Definition

Polyquaternium-10, also known as Quaternium-19, is a polymeric quaternary ammonium salt of hydroxyethyl cellulose reacted with a trimethyl ammonium substituted epoxide. There are various grades of Polyquaternium-10 with different average molecular weights generally ranging from 250,000 to 600,000. Polyquaternium-10 has three CAS numbers: 53568-66-4, 54351-50-7, and 55353-19-0.[1-3]

Chemical and Physical Properties

Polyquaternium-10 is a white granular powder with a characteristic amine odor. It is soluble in water and insoluble in alcohol and nonpolar organic sol-

vents. Polyquaternium-10 used in cosmetics has 0.5% maximum water insolubles, 1.7 to 2.2% nitrogen-containing components, 2% maximum ash (NaCl), and 6% maximum volatile material. The particle size specifications are 95% minimum through a 20 mesh filter and 85% minimum through a 40 mesh filter. The viscosity of a 2% aqueous solution (25°C) is between 60 and 150 centipoises.[4]

Polyquaternium-10 alters the surface tension of aqueous solutions of anionic surfactants. Addition of 1% and 2% Polyquaternium-10 lowered the surface tension of aqueous solutions of sodium lauryl sulfate, sodium tridecylbenzenesulfonate, and potassium laurate.[5]

Reactivity

Polyquaternium-10 is a cationic, surface-active polymer that is adsorbed by keratinous surfaces, such as hair and skin (stratum corneum). The adsorption of the polymer was not readily affected by pH in the range of 4 to 10. It undergoes slow hydrolytic cleavage outside this pH range. Sorption of Polyquaternium-10 to keratinous surfaces was decreased by the addition of electrolytes (salts), such as aluminum, iron, calcium, or sodium. Polyquaternium-10 is biologically degradable. The presence of ethyl alcohol or propylene glycol adds to the stability of Polyquaternium-10.[6-9]

Analytical Methods

The most common analytical method for quaternary ammonium compounds is colorimetric testing following separation by acid extraction.[10]

Method of Manufacture

Polyquaternium-10 is generally produced by reacting hydroxyethylcellulose with epichlorhydrin, followed by quaternization using trimethylamine. It is stable within a pH rane of 4 to 8.

Impurities

Inorganic impurities of Polyquaternium-10 used in cosmetics include water (up to 0.5%), nitrogen (1.7 to 2.2%), and ash (NaCl up to 2%). Information was not available on organic impurities of Polyquaternium-10.[4] Epichlorhydrin was not detected in any of six different Polyquaternium polymers analyzed with an average detection limit of about 0.5 ppm.[11] A maximum of 10.8 ppm Trimethylamine was detected in lots of Polyquaternium-10 that were produced and sold during 1985.[12]

USE

Purpose in Cosmetics

Polyquaternium-10 is used as a conditioner, emollient and viscosity controlling agent in cosmetics.[3,13,14]

Scope and Extent of Use in Cosmetics

Polyquaternium-10 is used primarily in hair care products, skin cleansers, and skin moisturizers in concentrations of ≤0.1%–5%. One hundred thirty-nine (139) of the voluntarily filed cosmetic product formulations were reported to the Food and Drug Administration to contain Polyquaternium-10.[15] The cosmetic product formulation data that are made available by the FDA are compiled through voluntary filing of such data in accordance with Title 21 part 720.4 of the Code of Federal Regulations.[16] 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 would be a fraction of that reported to the FDA. Data submitted within the framework of preset concentration ranges provide 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 2- to 10-fold error in the assumed ingredient concentration (Table 1).

Polyquaternium-10 has been generally or individually approved for use in cosmetic formulations marketed in Japan.[17]

Surfaces, Frequency, and Duration of Application

The hair care products containing Polyquaternium-10 are, for the most part, applied for a few minutes, then rinsed off. However, Polyquaternium-10 is incorporated in these products for its "substantivity" (sorption) and would be expected to remain in contact with the hair between treatments. Skin cleansers and moisturizers have the potential to remain in continuous contact with the skin and nails for extended periods of time.

BIOLOGY

Penetration, Sorption, and Permeation Through Stratum Corneum

Approximately 1 ml of a 5% (w/v) water solution of ^{14}C-Polyquaternium-10 (uniformly labeled on the pendant side chain) was applied to the backs of 12 Fischer 344 rats. The total dose of 4.0 ml/kg was occluded for the test period 1, 3, and 24 h. Six rats were placed in Roth-type glass metabolism cages designed for the separate collection of urine, feces, and expired air for the entire 24-h exposure period. The remaining 6 exposed animals were killed, 3 at 1 h and 3 at 6-h postexposure. Blood measured at 1 h and 3 h for the interim sacrifices and for the 6 material balance rats killed at 24 h had no radioactivity above background. There was no radioactivity above background in any of 9 tissues examined in the 6 animals that were killed at 24 h. Less than 0.02% of the administered dose was found in the urine and less than 0.1% in the feces; no radioactivity was recovered in CO_2. Of the 83.7% of the total dose that was recovered from the male rats, 75.2% was from the occlusive materials and 7.1% was found

TABLE 1. Product Formulation Data for Polyquaternium-10[15]

Product category	*Total no. of formulations in category*	*Total no. containing ingredient*	*No. of product formulations w concentration range (%*		
			Unreported concentration	*>1–5*	*>0.*
Bubble baths	475	1	–	–	
Mascara	397	5	–	–	
Hair conditioners	478	16	–	6	
Hair sprays (aerosol fixatives)	265	1	–	–	
Permanent waves	474	6	–	1	
Hair shampoos (noncoloring)	909	62	–	9	4
Tonics, dressings, and other hair grooming aids	290	4	–	–	
Wave sets	180	6	–	2	
Other hair preparations (noncoloring)	177	1	–	–	
Hair shampoos (coloring)	16	3	–	–	
Makeup bases	831	2	–	–	
Bath soaps and detergents	148	1	–	–	
Skin cleansing preparations (cold creams, lotions, liquids, and pads)	680	6	2	–	
Face, body, and hand skin care preparations (excluding shaving preparations)	832	8	–	–	
Moisturizing skin care preparations	747	12	1	–	
Night skin care preparations	219	1	–	–	
Paste masks (mud packs)	171	1	–	–	
Skin fresheners	260	1	–	–	
Wrinkle smoothers (removers)	38	1	–	–	
Other skin care preparations	349	1	–	–	
1981 TOTALS		139	3	18	8

in or around the skin at the dose site. The fraction of the applied material that did penetrate the skin amounted to less than 1.5% of the administered radioactivity. The investigators noted the low total recovery of the applied radioactivity; however, if the data were normalized to 100%, less than 1.75% of the applied dose would have penetrated the skin. The authors concluded that Polyquaternium-10 is unlikely to penetrate the human skin in toxicologically significant amounts.[18,19]

The anti-irritant effect of hydroxyl and quaternary ammonium compounds, including Polyquaternium-10, has been investigated in recent years. It has been hypothesized that the sorption properties of Polyquaternium-10 enable the polymer to block keratin reactive sites, thus reducing the topical and eye irritant effects of surfactants in shampoo and cleanser formulations.[20,21]

Several studies have investigated the passage of Polyquaternium-10 and surfactants, such as sodium lauryl sulfate, into and through isolated stratum corneum from the skin of fetal pigs, neonatal rats, and adult humans. The fetal pigskin was frozen, and on warming, the stratum corneum was gently separated from the underlying epidermis. Neonatal rat skin was removed following death by CO_2 inhalation. The skin was placed in a desiccator jar and exposed to ammonia vapor for 1–3 h, then put in water to remove the epidermis from the dermis. After 1 h the epidermis was recovered on a paper towel, and the malpighian layer was scraped off, leaving the stratum corneum to dry. The various preparations were exposed to ^{14}C-Polyquaternium-10 and/or surfactant (in aqueous solution) in vials or permeability cells[22] to quantify sorption and permeability and to evaluate the effects of the polymer on the preparations. The results indicated that Polyquaternium-10 slowly diffused into the outer layer of the stratum corneum (all three species) rather than forming multilayers on the surface. Although ionic surfactants did reduce polymer sorption, pretreatment of the stratum corneum with 1% Polyquaternium-10 greatly reduced the amount of surfactant that passed through the preparation. This reduction in permeation of surfactant supported the hypothesis that Polyquaternium-10 is an anti-irritant in the presence of ionic (i.e., irritant) surfactants. The kinetics of polymer/surfactant sorption and permeation indicated that the polymer did not act primarily as a barrier to penetration, but rather it helped to maintain the physical integrity of the stratum corneum preparation.

Pretreatment of the stratum corneum of neonatal rats with Polyquaternium-10 slightly increased the hydration of the membrane and reduced swelling after surfactant exposure.[2,9,23,24]

ANIMAL TOXICOLOGY

Oral Toxicity

Three lots of Polyquaternium-10 were tested for acute oral toxicity by intubation in rats. Three studies at maximum doses of 16 g/kg, 13.1 g/kg, 16 g/kg did not achieve the LD_{50}.[25–27]

The acute oral toxicity of 1.0% Polyquaternium-10 in a shampoo and a conditioner was tested by gavage. The LD_{50} of the two formulations was not reached at 5 g/kg.[28,29] Results are summarized in Table 2.

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