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8

Final Report on the Safety Assessment of Polyquaternium-11

Polyquaternium-11 is a quaternized copolymer of vinylpyrrolidone and dimethylamine ethylmethacrylate, and is used at concentrations up to 50% in a variety of hair care preparations.

The acute oral LD50 in test animals of high molecular weight Polyquaternium-11 is estimated to be greater than 12.8 g/kg; the LD50 for the low molecular weight polymer is calculated to be 6.2 g/kg. At concentrations of up to 50% in water, the raw ingredient produced no signs of skin or eye irritation. There was no evidence of dermal toxicity in subchronic tests nor in a maximization test for sensitization. In clinical studies, 1 of 19 subjects showed slight skin irritation after a 24-hour single insult skin patch with 9.5% Polyquaternium-11 in water. Repeated insult patch tests at concentrations up to 50% produced no instances of skin sensitization and only isolated instances of transient skin irritation. Clinical photoreactivity studies on both low and high molecular weight polymers showed no evidence of phototoxicity or photoallergenicity.

From the available information, it is concluded that Polyquaternium-11 is safe as a cosmetic ingredient in the present practices of use.

INTRODUCTION

Whereas Polyquaternium-11 is the singular ingredient under review in this report, two distinct forms of the material are available in industry: a low molecular weight form dissolved in alcohol (50 ± 2%) and a high molecular weight form dissolved in water (19% minimum). The undiluted polymer per se is not available for incorporation into cosmetic products, although the potential exists for evaporation of the vehicle prior to formulation. An attempt is made here to distinguish between the pure Polyquaternium-11 polymer and the diluted products found in the industry by referring to the latter as "commercial Polyquaternium-11." Since all available safety data pertain to the material that is supplied by the manufacturer (commercial Polyquaternium-11), calculations of concentrations and doses back to the pure Polyquaternium-11 polymer are made where appropriate to aid in the assessment of safety.

CHEMISTRY

Structure

Polyquaternium-11 is a copolymer of vinylpyrrolidone and dimethylamine ethylmethacrylate, partially quaternized with diethyl sulfate. The general reaction sequence is as follows:[1,2]

Properties

Polyquaternium-11 is supplied by the manufacturer as either a low molecular weight polymer in alcohol (50 ± 2% solids) or a high molecular weight polymer in water (minimum 19% solids).[3] Chemical and physical properties of the two commercial forms of Polyquaternium-11 are listed in Table 1. These values are typical of the commercial products, but they are not specifications.

Reactivity

No information was available on the chemical reactivity of Polyquaternium-11.

Analytical Methods

Methods for the determinations of viscosity, residual vinylpyrrolidone content, and nonvolatile solids content have been described.[1] Infrared[3] and ultraviolet[4] spectra are available for both the low and high molecular weight products.

Impurities

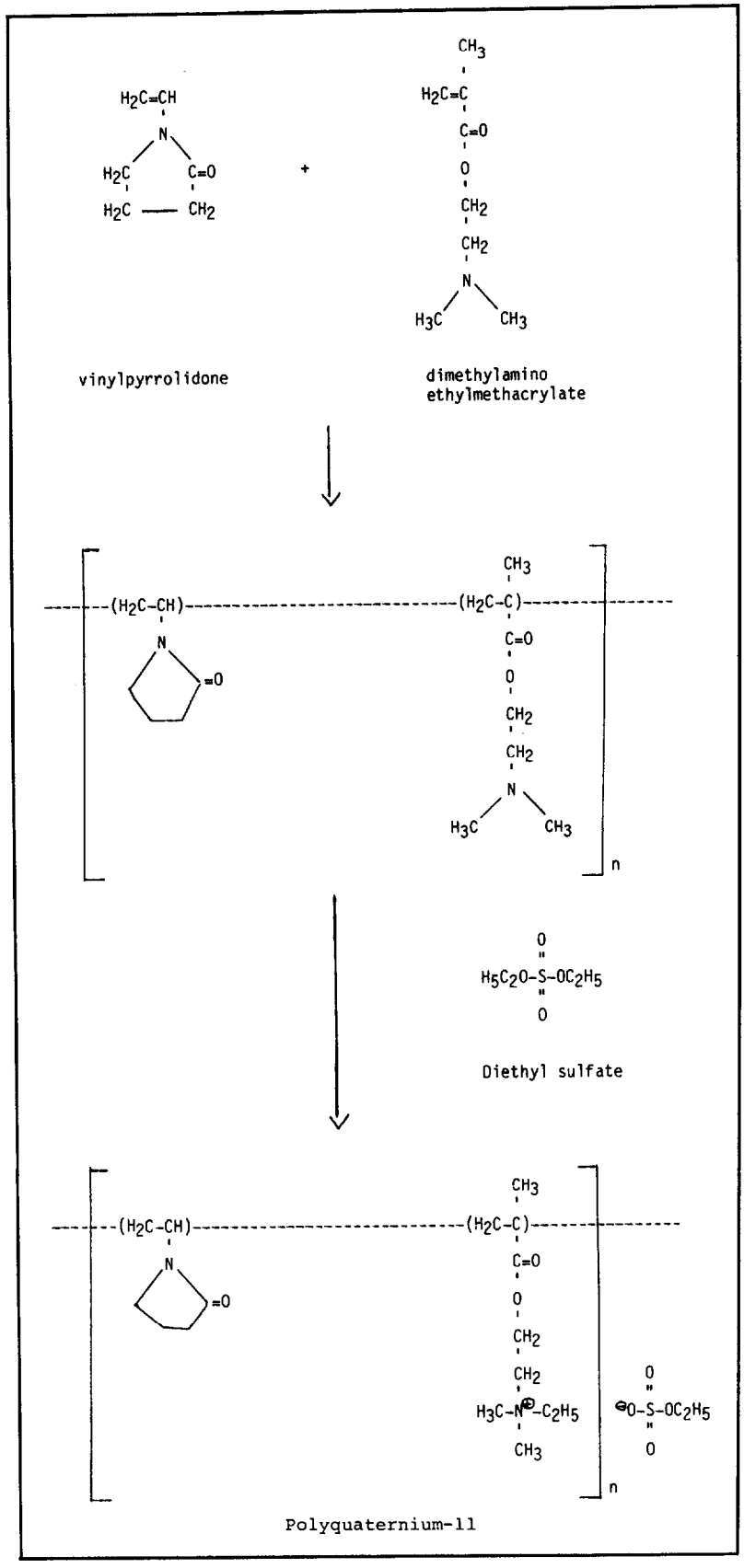
The low molecular weight and high molecular weight forms of Polyquaternium-11 are supplied in solution with ethanol (denatured with tertiary butyl alcohol and brucine, brucine sulfate, or quassin) and water, respectively. There are no known additives.[1,3] No information was available on the possible presence of nitrosamines.

Industry specifications for Polyquaternium-11 allow residual vinylpyrrolidone to a maximum concentration of 1.0%.[1,3] Free vinylpyrrolidone is a chemically

TABLE 1. Properties of Commercial Polyquaternium-11.[a]

	Low molecular weight polymer	*High molecular weight polymer*
Average molecular weight	<100,000	>1,000,000
Physical form (25°C)	Hazy, viscous liquid	Hazy, viscous liquid
Color	Light to dark straw	Light to dark straw
Vehicle	Alcohol	Water
Solids content	50 ± 2%	19% minimum
Relative viscosity (Ostwald-Fenske capillary viscometer)	2.5-3.5 (1% in anhydrous SD-40)	1.5-2.0 (0.1% in anhydrous SD-40)

[a]Data from Ref. 3.


vinylpyrrolidone
dimethylamino
ethylmethacrylate
Diethyl sulfate
Polyquaternium-11

highly reactive species; however, the residual monomer is unlikely to be present at significant concentrations in product formulations.

Polyquaternium-11 does not contain as an impurity diethylsulfate, an alkylating agent and a direct-acting carcinogen in rats; diethylsulfate is hydrolyzed quickly in air.[5] Upon quaternization of the copolymer, the nonalkylating agent monoethylsulfate is formed.

USE

Purpose in Cosmetics

The principal use of Polyquaternium-11 in cosmetic products is in hair care preparations. It is a film-forming resin that is absorbed onto the hair shaft. The benefits claimed with application to the hair include improvements in holding and curl retention at high humidities, hair strength and weight, manageability, luster, smoothness, lubricity, and moisture retention.[3]

Scope and Extent of Use in Cosmetics

Table 2 lists the product types and the number of product formulations containing Polyquaternium-11 as reported by the Food and Drug Administration (FDA) in 1976. Although an analysis by type of product at each concentration level was not available for the more recent 1979 FDA data, the 1979 totals for all product categories are also listed in Table 2 for comparison to the 1976 total figures.

The cosmetic product formulation computer printout which is made available by the FDA is compiled through voluntary filing of such data in accordance with Title 21 Part 720.4 of the Code of Federal Regulations.[8] 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 true 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 tenfold error in the assumed ingredient concentration.

In 1976, Polyquaternium-11 was listed in a variety of hair care preparations at concentrations up to 50%; it found only minimal use in other product categories. It is possible that some or all of the concentrations reported to the FDA by cosmetic formulators were those for the material that was supplied by the ingredient manufacturer. Since Polyquaternium-11 is supplied as a solute in an alcohol (50 ± 2% solids) or water (minimum 19% solids) vehicle, the concentrations of the polymer in cosmetic formulations may be from 19% to 50% of those shown in Table 2.

TABLE 2. Product Formulation Data.[a]

Product category[b]	Total no. containing ingredient	No. product formulations within each concentration range (%)[b]							
		Unreported concentration	>50	>25–50	>10–25	>5–10	>1–5	>0.1–1	≤0.1
Polyquaternium-11									
Hair conditioners	31	–	–		2	22	4	1	2
Hair sprays (aerosol fixatives)	2	–	–	–		–	2	–	–
Permanent waves	4	–	–	–		3	1	–	–
Hair rinses (noncoloring)	3	–	–	–		–	3	–	–
Hair shampoos (noncoloring)	5	–	–	–		–	–	5	–
Tonics, dressings, and other hair grooming aids	6	–	–	–		–	6	–	–
Wave sets	13	–	–	1	2	1	8	1	–
Other hair preparations (noncoloring)	9	–	–	–	2	–	5	1	1
Hair dyes and colors (all types requiring caution statement and patch test)	6	–	–	–	–	–	–	6	–
Hair rinses (coloring)	4	–	–	–	–	–	–	4	–
Hair bleaches	1	–	–	–	–	–	–	1	–
Shaving cream (aerosol, brushless, and lather)	4	–	–	–	–	–	–	4	–
Paste masks (mud packs)	1	–	–	–	1	–	–	–	–
1976 TOTALS	89	–	–	1	7	26	29	23	3
1979 TOTALS[c]	114	69	–	1	4	3	18	14	5

[a]Data from Ref. 6.

[b]Preset product categories and concentration ranges in accordance with federal filing regulations (21 CFR 720.4); see Scope and Extent of Use in Cosmetics.

[c]Data from Ref. 7.

Potential Interactions with Other Ingredients

Chemical interactions of Polyquaternium-11 with the other ingredients in cosmetic formulations have not been reported.

Vehicles Commonly Used

Denatured ethanol and water are the principal vehicles of low and high molecular weight Polyquaternium-11, respectively.[3]

Surfaces to Which Commonly Applied

Products containing Polyquaternium-11 are applied primarily to the hair. The ingredient finds limited use in products that are applied to the facial skin (Table 2).

Frequency and Duration of Application

The product formulation data[6] presented in Table 2 show that Polyquaternium-11 is contained in product formulations that are likely to be used no more than once a day. The resin films left by these products will remain in contact with the hair and scalp or facial skin for indefinite periods of time following each application. Daily or occasional use may extend over many years.

BIOLOGICAL PROPERTIES

General Effects

Antimicrobial[9,10] and antiheparin[11] activities have been attributed to quaternary ammonium polymers and their salts.

Although no information was available on the absorption, metabolism, storage, excretion, or any other general biological property of Polyquaternium-11, such polymers are generally considered to be biologically inert.

Animal Toxicology

Acute Studies

Oral Toxicity

Samples of low and high molecular weight Polyquaternium-11 in water, as well as six cosmetic formulations containing the ingredient, were evaluated for acute oral toxicity (Table 3). In each study, young adult albino rats or mice were fasted for 24 hours and administered a single dose of the test material by gastric intubation. They were then allowed free access to food and water for two weeks. The results and other details of these studies are summarized in Table 3. From these data, the acute oral LD50 of high molecular weight Polyquaternium-11 is greater than 12.8 g/kg; the LD50 for low molecular weight Polyquaternium-11 is calculated to be 6.2 g/kg.

Primary Skin Irritation

The potentials for primary skin irritation caused by samples of low and high molecular weight Polyquaternium-11 in water[20,21] and by five product formulations containing 0.19%–1.0% Polyquaternium-11 solids[22-26] were evaluated using the Draize rabbit skin patch test technique. In each study, the test material was applied and occluded for 24 hours, after which time the patch sites were graded for erythema and edema on the Draize scale. The results and other details of these studies are summarized in Table 4. The unformulated samples of Polyquaternium-11 in water, as well as the product formulations containing the ingredient, produced no signs of skin irritation.

Eye Irritation

The Draize rabbit eye irritation procedure or a modification of the test was used to evaluate samples of low and high molecular weight Polyquaternium-11[27,28] and six product formulations containing 0.19%–2.0% Polyquaternium-11 solids.[14,29-33] In each study, a 0.1 ml sample of the test material was instilled into one eye of each rabbit with no subsequent washing; the untreated eye served as a control. Treated eyes were examined and graded on the Draize eye irritation scale at 1, 2, 3, 4, and 7 days. The results and other details of these studies are summarized in Table 5. The unformulated samples of Polyquaternium-11 in water produced no signs of ocular irritation; product formulations containing the ingredient produced no more than mild, transient, conjunctival irritation.

Subchronic Studies

Dermal Toxicity

A commercial sample of high molecular weight Polyquaternium-11 (approximately 19% in water) was tested for cutaneous toxicity in a 28-day study. The sample was administered as a 25% (w/v) solution in water for an effective concentration of 4.75% Polyquaternium-11 solids. Doses of 2.0 ml/kg of the solution or approximately 0.10 g/kg of polymer were applied to the shaved backs of ten albino rabbits, five days a week, for a total of 20 applications. The skin of four animals received epidermal abrasions prior to the first treatment. A group of ten untreated animals served as a control. None of the animals died, and there were no untoward behavioral or systemic reactions. Hematologic studies, clinical blood chemistries, and urinalyses revealed no significant adverse reactions. No significant pathologic alterations were noted on gross and microscopic observations other than in the skin at the site of contact. The test material was slightly to mildly irritating to the skin with gross skin changes characterized by barely perceptible to pale red erythema and slight edema. Microscopic changes were characterized by acanthosis, hyperkeratosis, and parakeratosis.[34]

Skin Sensitization

The Magnusson-Kligman[35] guinea pig maximization procedure was used to evaluate the potential for skin sensitization to a low molecular weight commercial sample of Polyquaternium-11 (50% in alcohol). During the induction phase

TABLE 3. Acute Oral Toxicity.

Material tested[a]	*Conc. of Polyquaternium-11 (%)*	*Dose*	*Dose of Polyquaternium-11 (adjusted for dilution)*	*Animals*	*LD50*	*Comments*	*Ref.*
Polyquaternium-11, low molecular weight polymer	25 in water	16.0–40.0 g/kg	1.0–2.5 g/kg	5 rats at each of 5 dose levels	6.2 g/kg	Alcohol vehicle evaporated and solids redissolved in water	12
Polyquaternium-11, high molecular weight polymer	19 in water	25.1–64.0 ml/kg	4.8–12.2 ml/kg	5 rats at each of 5 dose levels	>12.2 ml/kg (>12.8 g/kg)	No deaths	13
Setting lotion, 10% high molecular weight commercial Polyquaternium-11	2.0 in product formulation	15.0 g/kg	0.3 g/kg	5 rats		LD50 not reached with dose administered	14
Hair conditioner, 2.0% low molecular weight commercial Polyquaternium-11	1.0 in product formulation	1.0–16.0 g/kg	0.01–0.16 g/kg	5 rats at each of 5 dose levels		No deaths; no signs of toxicity	15

Hair conditioner, 2.0% high molecular weight commercial Polyquaternium-11	0.38 in product formulation	1.0–16.0 g/kg	0.0038–0.061 g/kg	5 rats at each of 5 dose levels	No deaths; no untoward signs at product dosage levels up to 8.0 g/kg; at 16.0 g/kg the animals were lethargic and had diarrhea	16
Hair conditioner, 1.5% high molecular weight commercial Polyquaternium-11	0.3 in product formulation	15 g/kg	0.045 g/kg	5 rats	No deaths; no signs of toxicity	17
Shampoo, 1.0% high molecular weight commercial Polyquaternium-11	0.19 in product formulation	15 ml/kg	0.028 ml/kg	10 mice	No deaths	18
Setting lotion, 0.6% low molecular weight commercial Polyquaternium-11	0.3 in product formulation	5.0 g/kg	0.015 g/kg	10 rats	No deaths; no signs of toxicity	19

[a]Low molecular weight polymer supplied as 50% solution in alcohol; high molecular weight polymer supplied as 19%–20% solution in water. Molecular weight of polymer tested inferred from the reported concentration and vehicle of the material supplied.

TABLE 4. Primary Skin Irritation.

Material tested[a]	*Conc. of Polyquaternium-11 (%)*	*No. of rabbits*	*Primary irritation index (max = 8.0)*	*Comments*	*Ref.*
Polyquaternium-11, low molecular weight polymer	50 in water	6	0.0	Alcohol vehicle evaporated and solids redissolved in water No signs of irritation	20
Polyquaternium-11, high molecular weight polymer	19 in water	6	0.0	No signs of irritation	21
Hair conditioner, 2.0% low molecular weight commercial Polyquaternium-11	1.0 in product formulation	6	0.0	No signs of irritation	22
Hair conditioner, 2.0% high molecular weight commercial Polyquaternium-11	0.38 in product formulation	6	0.0	No signs of irritation	23
Hair conditioner, 1.5% high molecular weight commercial Polyquaternium-11	0.3 in product formulation	9	0.0	No signs of irritation	25
Setting lotion, 0.6% low molecular weight commercial Polyquaternium-11	0.3 in product formulation	6	0.0	No signs of irritation	24
Shampoo, 1.0% high molecular weight commercial Polyquaternium-11	0.05 in diluted product formulation	3	0.0	No signs of irritation; product diluted 1:3 prior to patching	26

[a]Low molecular weight polymer supplied as 50% solution in alcohol; high molecular weight polymer supplied as 19%–20% solution in water. Molecular weight of polymer tested inferred from the reported concentration and vehicle of the material supplied.

of the test, ten female albino guinea pigs each received the following paired 0.05 ml intradermal injections in the shaven skin of the back: (1) 50% aqueous Freund's Adjuvant; (2) 5% commercial Polyquaternium-11 in 50% aqueous Freund's Adjuvant; and (3) 5% commercial Polyquaternium-11 in propylene glycol. One week after the induction injections, a topical "booster" was administered as a 48-hour occlusive patch over the initial injection site with 0.5 ml of 25% commercial Polyquaternium-11 in petrolatum. Two weeks after the topical

TABLE 5. Acute Eye Irritation.

Material tested[a]	*Conc. of Polyquaternium-11 (%)*	*No. of rabbits*	*Results*	*Ref.*
Polyquaternium-11, low molecular weight polymer	50 in water	6	Alcohol vehicle evaporated and solids redissolved in water No signs of irritation	27
Polyquaternium-11, high molecular weight polymer	19 in water	6	No signs of irritation	28
Setting lotion, 10% high molecular weight commercial Polyquaternium-11	2.0 in product formulation	3	Transient conjunctival irritation on day 1; all eyes normal by day 2	14
Hair conditioner, 2.0% low molecular weight commercial Polyquaternium-11	1.0 in product formulation	6	Transient conjunctival irritation in all animals at 1 hour; all eyes normal by 24 hours	29
Hair conditioner, 2.0% high molecular weight commercial Polyquaternium-11	0.38 in product formulation	6	Transient conjunctival irritation in all animals at 1 hour; mostly clear by 24 hours; all eyes normal by 48 hours	30
Hair conditioner, 1.5% high molecular weight commercial Polyquaternium-11	0.3 in product formulation	6	No signs of irritation	32
Setting lotion, 0.6% low molecular weight commercial Polyquaternium-11	0.3 in product formulation	6	No signs of irritation	31
Shampoo, 1.0% high molecular weight commercial Polyquaternium-11	0.05 in diluted product formulation	3	No signs of irritation; product diluted 1:3 prior to instillation	33

[a]Low molecular weight polymer supplied as 50% solution in alcohol; high molecular weight polymer supplied as 19%–20% solution in water. Molecular weight of polymer tested inferred from the reported concentration and vehicle of the material supplied.

booster, all animals were challenged at a previously untreated site with 0.5 ml of 5% commercial Polyquaternium-11 in petrolatum under an occlusive patch for 24 hours. The challenged sites were graded for erythema at 24 and 48 hours after patch removal. A similar test procedure was conducted with one vehicle-treated negative control group and one phenylacetaldehyde-treated positive control group. Phenylacetaldehyde produced an expected strong allergic reaction; Polyquaternium-11 and negative control groups showed no evidence of allergic skin sensitization.[36]

Polyquaternium-11 was evaluated for skin sensitization in another test on albino guinea pigs. A 0.5 ml dose of the high molecular weight polymer at 19% in water was applied under an occlusive patch and left in contact with the skin for six hours. The insult was repeated once a week for three weeks. Two weeks after the last induction exposure, the animals were challenged with an occlusive patch at a virgin site. The investigator concluded that the material was not a sensitizer in this test; experimental data were not available for review.[37]

Inhalation

A 13-week inhalation toxicity study was performed on an aerosol of a hair conditioner containing 1.5% commercial Polyquaternium-11 (approximately 20% high molecular weight polymer in water). Groups of 12 hamsters and 12 rats were exposed in a dynamic chamber 4 hours per day, 5 days per week, to a mean product concentration of 9.9 mg/m^3; the effective final concentration of Polyquaternium-11 solids was approximately 0.03 mg/m^3. There were neither deaths nor adverse local or systemic effects in either species. Gross and microscopic observations revealed nothing in the lungs or other tissues examined that distinguished exposed from control animals.[38]

Special Studies

Unreacted vinylpyrrolidone monomer, which is allowed by industry specifications as an impurity in Polyquaternium-11 at concentrations up to 1.0%, was found to be nonmutagenic in three different assays. In the mouse lymphoma forward mutation assay, concentrations up to 5.0 μl/ml did not induce a significant change in mutation frequency at the TK locus of L5178Y cells in the absence or presence of rat liver S-9 microsomal activation.[39] In the Balb/3T3 in vitro transformation assay, vinylpyrrolidone induced no significant increase in transformed foci over the applied concentration range of 0.5–0.1 μl/ml. This concentration range produced 52.3%–83% survival in the cytotoxicy test. The test material was considered to be mutagenically inactive.[40] In the primary rat hepatocyte unscheduled DNA synthesis assay, vinylpyrrolidone induced no detectable activity over an applied concentration range of 9.09–0.284 μl/ml. This concentration range produced a cell survival rate from 6.2% to 84.5% at 24 hours after treatment, whereas exposure to 18.2 μl/ml was completely lethal. The material was considered to be inactive as a genotoxic agent in this assay system.[41]

Data were not available on mutagenicity, carcinogenicity, or teratogenicity for the low or high molecular weight forms of Polyquaternium-11.

Clinical Assessment of Safety

Primary Skin Irritation

A 24-hour occlusive patch test procedure was used to evaluate the primary skin irritation caused by an aqueous solution of Polyquaternium-11[42] and by two product formulations containing Polyquaternium-11.[14,43] The results and other details of these studies are summarized in Table 6. Polyquaternium-11 at 9.5% in water produced only a slight degree of irritation in 1 of 19 subjects. A product formulation containing high molecular weight Polyquaternium-11 at

TABLE 6. Clinical Studies on Polyquaternium-11.

Test	*Material tested*[a]	*Conc. of Polyquaternium-11 (%)*	*Method*	*No. of subjects*	*Comments*	*Ref.*
Primary skin irritation	Polyquaternium-11, high molecular weight polymer	9.5 in 50% aqueous dilution of commercial raw ingredient	24-hour occlusive patch	19	One subject showed slight irritation (score = 1.0 out of 4.0 max.); all others exhibited no signs of irritation	42
	Setting lotion, 10% high molecular weight commercial Polyquaternium-11	2.0 in product formulation	24-hour occlusive patch	100	"Negative"	14
	Hair conditioner, 1.5% high molecular weight commercial Polyquaternium-11	0.3 in product formulation	24-hour occlusive patch	29	All subjects showed barely perceptible to mild irritation; PII = 0.52/4.0	43

TABLE 6. (Continued.)

Test	*Material tested*[a]	*Conc. of Polyquaternium-11 (%)*	*Method*	*No. of subjects*	*Comments*	*Ref.*
Skin sensitization	Polyquaternium-11, low molecular weight polymer	50 in alcohol	Draize–Shelanski Repeated Insult Patch Test; semiocclusive	150	Isolated, transient occurrences of skin irritation during induction phase (3 of 1421 patches); no skin sensitization	46
	Polyquaternium-11, high molecular weight polymer	19 in water	Draize–Shelanski Repeated Insult Patch Test; semiocclusive	150	Isolated, transient occurrences of skin irritation during induction phase (4 of 1421 patches); no skin sensitization	46
	Polyquaternium-11, high molecular weight polymer	9.5 in 50% aqueous dilution of commercial raw ingredient	Draize–Shelanski Repeated Insult Patch Test; occlusive	201	"Essentially nonirritating" during induction phase; no skin sensitization	47
	Hair conditioner, 5% high molecular weight commercial Polyquaternium-11	0.5 in 50% aqueous dilution of product formulation	Draize–Shelanski Repeated Insult Patch Test; occlusive	99	Mild primary irritation during induction phase; no evidence of skin sensitization at challenge with 25% aqueous dilution	48
Clinical use test	Hair condition, 5% high molecular weight commercial Polyquaternium-11	1.0 in product formulation	3 weeks normal use with additional 3-week use of control product	54	Skin and scalp effects comparable to those of control product; subjective irritation reported by 5 subjects; no empirical data available	49

[a]Low molecular weight polymer supplied as 50% in alcohol; high molecular polymer supplied as 19%–20% solution in water. Molecular weight of polymer tested inferred from the reported concentration and vehicle of the material supplied.

2.0% produced no irritation in 100 subjects; another formulation containing 0.3% high molecular weight Polyquaternium-11 produced up to mild skin irritation in 29 subjects.

Skin Sensitization

The Draize–Shelanski Repeated Insult Patch Test[44,45] or a modification of the test was used to evaluate Polyquaternium-11 at concentrations of 9.5% (201 subjects) and 19% (150 subjects) in water[46,47] and 50% (150 subjects) in alcohol.[46] The induction phase of the procedure consisted of a series of nine 24-hour occlusive or semiocclusive patch applications to the same site over a period of three consecutive weeks. A single challenge patch was applied to the original contact site and/or a virgin site after a 10- to 14-day rest period. The results and other details of these studies are summarized in Table 6. Polyquaternium-11 at concentrations of 9.5%–50% produced only minimal skin irritation during the induction phase of the procedure; there were no instances of skin sensitization.

A 50% aqueous dilution of a hair conditioner containing 1.0% Polyquaternium-11 was also evaluated in a modified Draize-Shelanski Repeated Insult Patch Test on 99 subjects. The results and other details of this study are summarized in Table 6. The product produced mild primary skin irritation but no skin sensitization.[48]

Photoreactivity

The ultraviolet spectra of the different forms of Polyquaternium-11 are available.[4] The low and high molecular weight forms dissolved in methanol at concentrations of 74 mg/l and 181 mg/l, respectively, produced no indication of significant ultraviolet absorption. At 50% in methanol, the low molecular weight polymer showed no significant absorption, while the high molecular weight polymer showed a questionably significant peak at 284 nm. The FDA product formulation data include only one formulation in the >25%–50% concentration range (see Table 2).

Clinical photoreactivity studies on commercial samples of both low (50 ± 2% solids in alcohol) and high (19% solids in water) molecular weight Polyquaternium-11 have been conducted.[50,51] Each of the test materials was applied to the inner aspect of the forearms of 31 women ranging in age from 20 to 63. One forearm was designated as the irradiated site and the other as the control (nonirradiated) site. Approximately 0.2 ml of the test material was applied to a Webril occlusive patch; patches were applied to the contact sites and allowed to remain in place for 24 hours. Patches were removed, and test sites were exposed to 15 minutes of nonerythrogenic ultraviolet radiation for a total UV-A light dosage of 4400 $\mu W/cm^2$. The ultraviolet light source consisted of four GE F450 BL blacklight fluorescent tubes held at a distance of 10 cm; this light source had a wavelength of 320–400 nm. (There was no filter employed.) This procedure of patching followed by irradiation was repeated Monday, Wednesday, and Thursday until ten exposure were completed. After a 10- to 13-day rest period, patches and irradiation were again performed on virgin, adjacent sites. The results of these studies indicated that the low and high molecular weight forms of

Polyquaternium-11 were neither phototoxic nor photoallergenic in the assays employed.

Clinical Use

A hair conditioner containing 1.0% Polyquaternium-11 was used together with a test shampoo by a panel of 54 subjects for a three-week period. Dermatologic exams and subjective evaluations of irritation and gentleness were compared to those made during a three-week period of control shampoo and conditioner use. The results and other details of this study are summarized in Table 6. The test shampoo and conditioner effects did not differ from the control products in any significant way.[49]

SUMMARY

Polyquaternium-11 is a quaternized copolymer of vinylpyrrolidone and dimethylamine ethylmethacrylate. It is reported by the FDA to be used at concentrations up to 50% in a variety of hair care preparations; it finds very limited use in other product categories. Since Polyquaternium-11 is supplied solely in the form of a solution at concentrations up to 50% in alcohol (low molecular weight polymer) or 19% in water (high molecular weight polymer), the actual concentrations of the polymer in cosmetic formulations may be less than those reported by the FDA.

Three different assay systems showed the vinylpyrrolidone monomer to be nonmutagenic; there is some indication that unreacted vinylpyrrolidone may be present as an impurity, but the residual monomer is unlikely to be present at significant concentrations in product formulations. It is recognized that the vinylpyrrolidone monomer is a chemically reactive species, and the safety evaluation of Polyquaternium-11 is with the understanding that the monomer is present only in biologically insignificant amounts.

In rats, the acute oral LD50 of high molecular weight Polyquaternium-11 is estimated to be greater than 12.8 g/kg; the LD50 for the low molecular weight polymer is calculated to be 6.2 g/kg. At concentrations of up to 50% in water, the raw ingredient produced no signs of skin or eye irritation in Draize rabbit irritation tests. There was no evidence of dermal toxicity other than local skin changes in a 28-day subchronic study with rabbits. The Magnusson-Kligman guinea pig maximization test and another guinea pig sensitization procedure produced no evidence of allergic skin sensitization. A 13-week subchronic inhalation study showed no toxic effects for a product formulation containing a final aerosolized Polyquaternium-11 concentration of 0.03 mg/m^3.

In clinical studies, 1 of 19 subjects showed slight skin irritation after a 24-hour single insult skin patch with 9.5% Polyquaternium-11 in water. A product formulation containing the ingredient at 2.0% produced no irritation; another formulation containing 0.3% produced up to mild irritation. A number of Draize-Shelanski repeated insult patch tests were conducted on Polyquaternium-11 at concentrations of up to 50%; there were no instances of skin sensitization and only isolated instances of transient skin irritation with both low and high

molecular weight polymers in a total of 450 subjects. Clinical photoreactivity studies on both low and high molecular weight polymers showed no evidence of phototoxicity or photoallergenicity. The ultraviolet absorbance spectrum of high molecular weight Polyquaternium-11 at a high (50%) concentration indicated some absorption at 284 nm, which is of questionable clinical significance with regard to photoreactivity; the FDA product formulation data included only one formulation in the > 25%–50% concentration range. A clinical use test on a product formulation containing 1.0% Polyquaternium-11 showed the product to be comparable in dermatologic effects to a similar control product; both produced some subjective reports of scalp irritation.

CONCLUSION

From the available information, the Panel concludes that Polyquaternium-11 is safe as a cosmetic ingredient in the present practices of use.

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REFERENCES

1. COSMETIC, TOILETRY AND FRAGRANCE ASSOCIATION (CTFA). (Oct. 1980). Submission of unpublished data. CTFA Cosmetic Ingredient Chemical Description.*
2. ESTRIN, N.F. (ed.). (1977). *CTFA Cosmetic Ingredient Dictionary,* 2nd ed. Washington, DC: Cosmetic, Toiletry and Fragrance Assoc.
3. GAF. (1970). Gafquat quaternary polymers, Publication No. 2302-005, IR Spectra attached. New York: GAF Corp.*
4. CTFA. (Jan. 25, 1982). Submission of unpublished data. U-V absorbance spectra, Quaternium-23 and PVP/VA.
5. INTERNATIONAL AGENCY FOR RESEARCH ON CANCER. (1974). Diethyl Sulfate IARC Monographs **4,** 277–81.
6. FOOD AND DRUG ADMINISTRATION (FDA). (Aug. 31, 1976). Cosmetic product formulation data. FDA Computer Printout. Washington, DC.
7. FDA. (June 20, 1979). Cosmetic product formulation data. Computer Printout. Washington, DC.
8. CODE OF FEDERAL REGULATIONS. (1979). Title 21. Washington, DC: U.S. Government Printing Office.
9. PANARIN, E.F., SOLOVSKII, M.V., and EKZEMPLYAROV, O.N. (1971–72). Synthesis and antimicrobial properties of polymers containing quaternary ammonium groups. Pharm. Chem. J. **5**(7), 406–8.
10. SOLOVSKII, M.V., PANARIN, E.F., VERSHININA, T.M., and KROPACHEV, V.A. (1974). Synthesis and antimicrobial properties of monomeric and polymeric quaternary ammonium salts based on aminoalkyl esters of methacrylic acid. Pharm. Chem. J. **8**(6), 347–50.
11. EFIMOV, V.S., GULYAEVA, ZH.G., MEN'SHOVA, G.I., RAZVODOVSKII, E.F., ZEZIN, A.B., and LAKIN, K.M. (1974). Study of antiheparin activity of polymeric quarternary ammonium salts polybrene analogs. Farmakol. Toksikol. (Moscow) **37**(6), 688–92.

*Available upon request: Administrator, Cosmetic Ingredient Review, Suite 810, 1110 Vermont Ave., N.W., Washington, DC 20005

12. FOOD AND DRUG RESEARCH LABS (FDRL). (April 28, 1969). Submission of unpublished data by CTFA. Acute oral toxicity.*
13. FDRL. (March 31, 1970). Submission of unpublished data by CTFA. Acute oral toxicity.*
14. CTFA. (1975). Submission of unpublished data. CIR safety data submission.*
15. BIOSEARCH LABS. (June 27, 1978). Submission of unpublished data by CTFA. Acute oral toxicity.*
16. BIOSEARCH LABS. (Dec. 12, 1978). Submission of unpublished data by CTFA. Acute oral toxicity.*
17. CTFA. (March 28, 1978). Submission of unpublished data. CIR safety data test summary, acute oral toxicity.*
18. LEBERCO LABS. (Sept. 27, 1977). Submission of unpublished data by CTFA. Acute oral toxicity.*
19. BIOSEARCH LABS. (Sept. 14, 1979). Submission of unpublished data by CTFA. Acute oral toxicity.*
20. FDRL. (April 28, 1969). Submission of unpublished data by CTFA. Primary skin irritation.*
21. FDRL. (March 31, 1970). Submission of unpublished data by CTFA. Primary skin irritation.*
22. BIOSEARCH LABS. (June 27, 1978). Submission of unpublished data by CTFA. Primary skin irritation.*
23. BIOSEARCH LABS. (Dec. 12, 1978). Submission of unpublished data by CTFA. Primary skin irritation.*
24. BIOSEARCH LABS. (Sept. 14, 1979). Submission of unpublished data by CTFA. Primary skin irritation.*
25. CTFA. (March 28, 1978). Submission of unpublished data. CIR safety data test summary, skin irritation.*
26. LEBERCO LABS. (Sept. 23, 1977). Submission of unpublished data by CTFA. Primary skin irritation.*
27. FDRL. (April 28, 1969). Submission of unpublished data by CTFA. Eye irritation study.*
28. FDRL. (March 31, 1970). Submission of unpublished data by CTFA. Eye irritation study.*
29. BIOSEARCH LABS. (June 27, 1978). Submission of unpublished data by CTFA. Primary eye irritation.*
30. BIOSEARCH LABS. (Dec. 12, 1978). Submission of unpublished data by CTFA. Primary eye irritation.*
31. BIOSEARCH LABS. (Sept. 14, 1979). Submission of unpublished data by CTFA. Primary eye irritation.*
32. CTFA. (March 28, 1978). Submission of unpublished data. CIR safety data test summary, eye irritation.*
33. LEBERCO LABS. (Sept. 26, 1977). Submission of unpublished data by CTFA. Eye irritation.*
34. INDUSTRIAL BIO-TEST LABS (IBTL). (Sept. 24, 1973). Submission of unpublished data by CTFA. 28-day subacute dermal toxicity study.*
35. MAGNUSSON, B. and KLIGMAN, A.M. (1969). The identification of contact allergens by animal assay. The guinea pig maximization test. J. Invest. Dermatol. **52**(3), 268–76.
36. CTFA. (Jan. 5, 1978). Submission of unpublished data. Guinea pig allergy study.*
37. IBTL. (March 29, 1973). Submission of unpublished data by CTFA. Skin sensitization tests in guinea pigs.*
38. CTFA. (May 10, 1979). Submission of unpublished data. CIR safety data test summary, 13-week inhalation study.*
39. LITTON BIONETICS. (Feb. 1980). Submission of unpublished data by CTFA. Mutagenicity evaluation of V-Pyrol (N-Vinyl-2-Pyrrolidone) in the mouse lymphoma forward mutation assay, final report.
40. LITTON BIONETICS. (April 1980). Submission of unpublished data by CTFA. Evaluation of V-Pyrol (N-Vinyl-2-Pyrrolidone) in the *in vitro* transformation of Balb/3T3 cells assay, final report.
41. LITTON BIONETICS. (April 1980). Submission of unpublished data by CTFA. Evaluation of V-Pyrol (N-Vinyl-2-Pyrrolidone) in the primary rat hepatocyte unscheduled DNA synthesis assay, final report.
42. CTFA. (May 3, 1973). Submission of unpublished data. Clinical evaluation report.*
43. CTFA. (March 10, 1979). Submission of unpublished data. CIR safety data test summary, human patch test.*
44. DRAIZE, J.H. (1955). Food Drug Cosmetic Law J. **10,** 722.
45. SHELANSKI, H.A. and SHELANSKI, M.V. (1953). Proc. Sci. Toilet Goods Assoc. **20,** 46.
46. TOXIGENICS. (Jan. 13, 1981). Submission of unpublished data by CTFA. Human repeated insult patch test.*
47. HILL TOP RESEARCH LABS. (Nov. 8, 1973). Submission of unpublished data by CTFA. Repeated insult patch test.*
48. RESEARCH TESTING LABS. (April 30, 1980). Submission of data by CTFA. Human patch study.*
49. CTFA. (Dec. 17, 1979). Submission of unpublished data. Clinical use test.*
50. FDRL. (March 16, 1982). Submission of unpublished data by CTFA. Photoallergy test of low molecular weight Quaternium-23.*
51. FDRL. (March 16, 1982). Submission of unpublished data by CTFA. Photoallergy test of high molecular weight Quaternium-23.*