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2

Final Report on the Safety Assessment of Shellac

Cosmetic-grade Shellac is a mixture of hydroxyaliphatic and alicyclic acids and their polyesters. It is used in cosmetic formulations at concentrations up to 25%.

Shellac had an LD_{50} of greater than 5 g/kg in rats. Results of acute animal toxicity studies using cosmetic formulations containing up to 6% Shellac indicated no adverse effects upon oral (rats), dermal (rabbits), ocular (rabbits), and respiratory tract (rabbits) exposure. Chronic inhalation of a Shellac hair spray formulation by rabbits produced no observable toxicity. No treatment-related toxic or pathologic effects were observed when concentrations of Shellac up to 10,000 ppm were fed to rats in a subchronic study.

Ames' mutagenicity assays, with and without metabolic activation, were negative.

Clinical assessment of safety of cosmetic formulations containing up to 6% Shellac indicated no measurable irritation and absence of sensitization and photosensitization.

It is concluded that cosmetic-grade Shellac is safe for use in cosmetic formulations at concentrations up to 6%, the maximum concentration tested.

CHEMICAL AND PHYSICAL PROPERTIES

Source

Lac is the hardened resinous secretion of a tiny-scale insect renamed *Kerria lacca* (Kerr)[1] (Fam. Coccidae[2]) (Synonyms: *Laccifer lacca* [Kerr] and *Tachardia lacca*[1]). The secreted lac, called "sticklac," contains lac resin, erythrolaccin, wax, insect debris, wood materials, sand, dust, and water-soluble impurities. The semirefined seedlac of commerce is the yellowish granular material obtained from the processing of sticklac.[1,3]

Composition

The Shellac (CAS Number: 9000-59-3) used by the food industry is further processed by either of two methods: mechanical process (heat or solvent) yielding "Machine Made or Orange Shellac" or chemical bleaching process (Na_2CO_3, NaOCl) yielding "Bleached Shellac."[4] Food-grade shellacs are divided into two

basic types: wax-containing and wax-free. Thus, four food-grade Shellacs are available, distinguished by method of processing and by wax content (Table 1). All four types of Shellac must have less than or equal to (≤) 1.5 ppm arsenic, ≤10 ppm heavy metal content (e.g., Pb), and must pass a specified test for rosin.[5]

TABLE 1. Processed Food-grade Shellacs

	Orange shellac	*Dewaxed orange shellac*	*Regular bleached shellac*	*Refined bleached shellac*
Description	Mechanical process Wax-containing	Mechanical process Wax-free	Chemical process Wax-containing	Chemical process Wax free
Acid value	68–76	71–79	73–89	75–91
Arsenic (ppm)	≤1.5	≤1.5	≤1.5	≤1.5
Rosin	None	None	None	None
Heavy metals (e.g., Pb)(ppm)	≤10	≤10	≤10	≤10
Moisture (%)	1–1.5	1–1.5	3.0–6.0	3.0–6.0
Wax (%)	4–4.5	0–0.2	4.0–5.5	0–0.2
Ash (%)	0.3–0.5	0.1–0.4	0.5–0.7	0.3–0.5
Hot alcohol insoluble (%)	0.1–0.5	0.0–0.1	0.5–0.7	0.1–0.2

The cosmetic industry uses Refined, Wax-Free Bleached Shellac (comparison of values in Cosmetic Ingredient Chemical Description, Table 2)[6–8] (Fig. 1).

Shellac wax and erythrolaccin, the yellow material, comprise approximately 6% of Shellac. Their removal yields lac resin that has soft (30%) and hard (70%) components.[9] Mild alkaline hydrolysis of this resin results in a complex mixture of hydroxy acids of aliphatic and alicyclic nature and their polyesters. The composition of the hydrolysate is dependent on the lac source and the time of collection.[10]

The major component of the aliphatic fraction is aleuritic acid, constituting approximately as much as 40% of the hydrolysate and accompanied by a large number of related carboxylic acids.[2,10] The sesquiterpenic acids make up the alicyclic fraction of Shellac (Table 3).

Other components of lac (Table 3) have been identified and partially characterized. Erythrolaccin, the yellow matter insusceptible to NaOCl bleaching treatment is 1,2,5,7-tetrahydroxy-4-methylanthraquinone.[3] Faurot-Bouchet and Michel[11] isolated, quantified, and partially identified components of shellac wax (Table 3). The hydroxy fatty acids, aleuritic acid (Fig. 2, melting point 100–101°C), butolic acid (Fig. 2, melting point 54–55°C), and kerrolic acid (Fig. 2, melting point 132°C) have been described by Cockerman and Levin.[12] Sesquiterpenic acids resembling shellolic and jalaric acid include epi-laccishellolic, epi-shellolic, lakshollic, and epi-lakshollic acids, differing from each other by methyl, aldehyde, hydroxymethyl, and carboxyl substituents to the basic ringed structure.

TABLE 2. Cosmetic Ingredient Chemical Description[6]

Test	*Typical range*
Identification	Positive: Close match to a standard IR spectrum with no indication of foreign materials
Acid value	95 maximum
Saponification value	250 maximum
Ester value	150–157
Iodine value	10 maximum
Moisture	6.0% maximum
Ash	0.3% maximum
Alcohol insolubles	0.1% maximum
Chlorides (as NaCl)	0.08–0.15%
Combined chlorine (as Cl)	2.0–2.6%
Sulfates (as Na_2SO_4)	0.07–0.1%
Wax	0.2% maximum

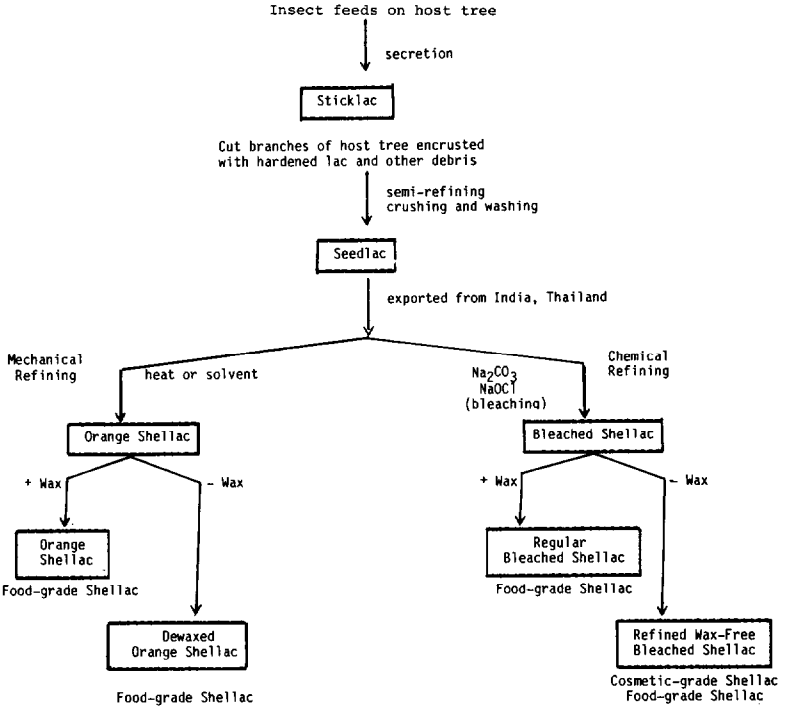


FIG. 1. Processing of lac.

TABLE 3. Substances Identified in Shellac or Shellac Hydrolyzates[9][a]

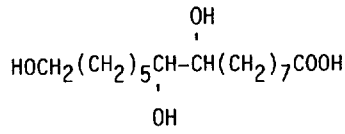
Fraction	*Shellac (%)*	*Substance*	*Approximate % of fraction*
Color	1	Erythrolaccin (yellow)	100
		Laccaic acid (red)	
Wax	5	Hydrocarbons	2
		Heptacosane (42)[b]	
		Nonacosane (35.1)	
		Hentriacontane (13.4)	
		C_{26}, C_{28}, C_{30}, C_{32}, C_{33}(Trace–4.1)	
		Acids	21
		C_{28} (18.9), C_{30} (25.1), C_{32} (27.2), C_{34} (17.6)	
		Traces of homologs	
		Fatty alcohols	77
		Octacosanol (66.6)	
		C_{26} (0.6), C_{30} (21), C_{32} (9), C_{34} (2.8)	
Lac resin	94	Sesquiterpenic acids	
		Jalaric acid	27
		Shellolic acid	2–8
		Epishellolic acid	
		Laksholic acid	
		Epilaksholic acid	
		Aliphatic acids	
		Aleuritic acid	45
		(9,10,16-trihydroxypalmitic acid)	
		10,11,15- and 8,9,16-trihydroxypalmitic acids	
		Butolic acid	5–8
		Kerrolic acid	1
		Tetradecanoic, hexadecanoic, octadecanoic, tetradecenoic, hexadecenoic, octadecenoic, 6-oxotetradecanoic, 16-hydroxyhexadec-9-*cis*-enoic, *threo*-9,10-dihydroxytetradecanoic, and *threo*-9,10-dihydroxyhexadecanoic acids	7
		Uncharacterized substances	7–12

[a]Reproduction of FASEB summary table in FDA Final Report on Shellac and Shellac Wax. Data summarized from Cockeram and Levine,[12] Faurot-Bouchet and Michel,[11] Markley,[13] Misra and Sengupta,[3] Singh et al.,[14] and Yates and Field.[2] The composition of lac resin is variable and dependent on conditions of preparation.

[b]Values in parentheses are the percentage of substance in the subfraction. For example, heptacosane comprises 42% of the hydrocarbons of the wax fraction.

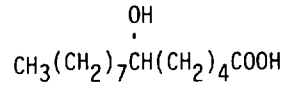
Aleuritic acid, or DL-erythro-9,10,16-trihydroxyhexadecanoic acid, with a molecular weight of 304.42 exists as crystals from dilute ethanol with a melting point of 100–101°C.

Jalaric acid, a major sesquiterpenic acid in Shellac (30% in Shellac)[3] is distinguished from shellolic acid, its oxidation product, by a secondary aldehyde function rather than a secondary carboxyl function (Fig. 3: R = –CHO jalaric acid; R = –COOH shellolic acid).



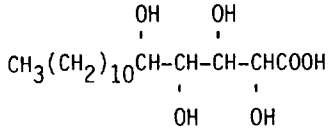
Aleuritic Acid

$C_{16}H_{32}O_5$; MW 304.42



Butolic Acid (6-hydroxytetradecanoic acid)

$C_{14}H_{28}O_3$; MW 244.38



Kerrolic Acid (2,3,4,5-tetrahydroxyhexadecanoic acid)

$C_{16}H_{32}O_6$; MW 332.44

FIG. 2. Structures of some aliphatic acids.

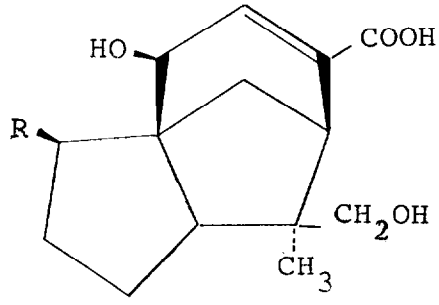


FIG. 3. Sesquiterpenic acid structure.

Jalaric acid R = $-CHO$
$C_{15}H_{20}O_5$; MW 280.33
Shellolic acid R = $-COOH$
$C_{15}H_{20}O_6$; MW 296.33

Shellolic acid is crystalline and has a melting point ranging from 204°C to 207°C. Its infrared absorption bands in potassium bromide are at 2.90, 3–4, 5.81, and 6.16 μ.[14] An ultraviolet absorption maximum for the dimethyl ester of shellolic acid in ethanol is at a wavelength of 231 nm (ϵ 6200).[10] Shellolic acid stereochemistry has been investigated by Yates and Field.[2,15]

The native form of the pure lac resin molecule has a molecular weight of 2095 ± 110 (osmometric method), which contains four terpene acids (mostly jalaric acid) and four aleuritic acid units in repeating ester linkage (Fig. 4).[14]

The proposed structure for lac resin only represents the average situation, since the molecule may not always be homogeneous with respect to sequence or ratio of jalaric acid to other sesquiterpenic acid substitutes.[14]

Physical Properties

Misra and Sengupta[3] provide a comprehensive report of the physical and chemical constants of varied forms of Shellac and lac resin (Table 4).

Shellac is soluble in alcohol (up to 85–95%, w/w); 13–15% in ether, 10–20% in benzene; 2–6% in petroleum ether; and sparingly soluble in oil of turpentine. Aqueous Shellac solutions can be prepared by neutralization with ethanolamines, alkalies, or borax.[10] The cosmetic industry's alcohol-based and water-based Shellac solutions are usually adjusted to pH 8–9 with one or more of the following bases: morpholine, borax, triethanolamine, aminomethylpropanol, aminomethylpropanediol, aminoethylpropanediol, tri-isopropylamine, or dodecylamine.[8,16]

Analytical Methods

Shellac may be identified and quantified by gas chromatography (thermal conductivity detection) after methyl esterification.[2,17] Infrared spectrophotometry for functional group identification and proton magnetic resonance spectroscopy[14] may also be used.

Shellac's extraction and gravimetric analysis in confectionery is described in the A.O.A.C. Official Methods.[18] Various spectrometric tests for Shellac involve chemical reactions that produce color and/or fluorescence in ultraviolet light.[19,20]

Stability

Dry Shellac becomes thermoplastic with age, and Shellac in alcohol solution tends to esterify, producing a soft and tacky resin with slow solvent release. The rate of esterification was found to be dependent on temperature and Shellac type; internal polymerization with heat was reversed by hydration and autoclaving.[4]

While Orange Shellacs have excellent thermal stability, Bleached Shellacs polymerize rapidly even at room temperature.[4] The reason for this difference in thermal stability is due to the instability of the O-Cl bond. The liberation of Cl_2 increased the acidity of Bleached Shellac solutions, which accelerated the esterification. Thus, all Shellacs, especially Bleached Shellac, should be stored in a very cool place, preferably refrigerated and away from all heat, including sunlight.[4]

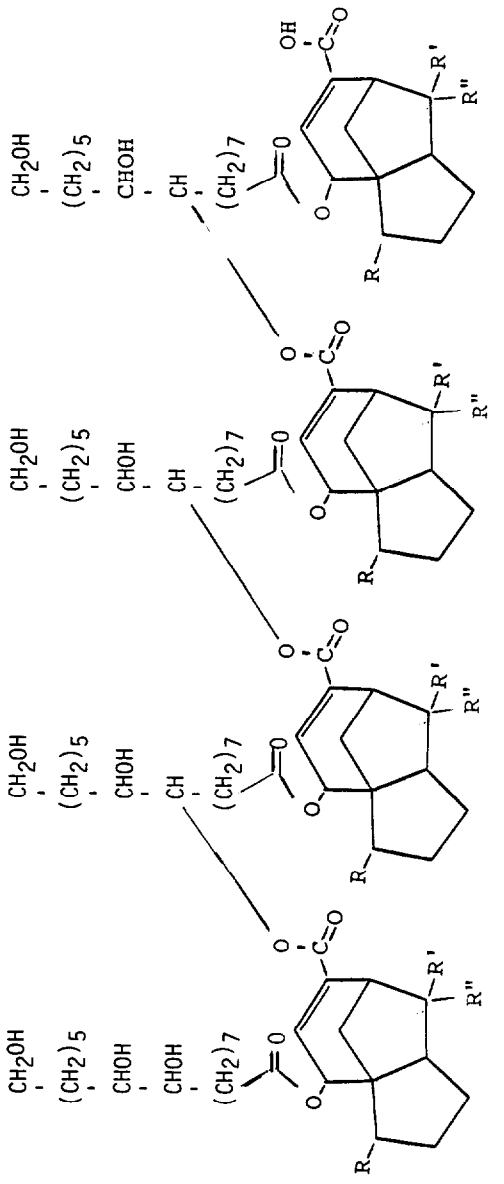


FIG. 4. Lac resin molecule. MW 2095 ± 110 (Singh et al., 1974[14]).
R = $-CHO/-COOH$ (Jalaric/shellolic)
R′ = $-CH_2OH$
R″ = $-CH_3$

TABLE 4. General Physical Properties and Chemical Constants[a]

Property	*Shellac*	*Dewaxed shellac*	*Bleached shellac*	*Hard or pure resin*	*Soft resin*
Molecular weight, methods					
Rastis	952–1143	– – –	914–974	1900–2000	513–556
Osmometric	– – –	– – –	– – –	1800–1857(3)	480–489
	– – –	– – –	– – –	2095 ± 110(14)	– – –
Acid value and basicity	– – –	– – –	– – –	1918–1932	535
Molecular volume, ml	– – –	1.59×10^{-21}	– – –	2.69×10^{-21}	9.97×10^{-21}
Viscous volume,[b] ml	– – –	7.623×10^{-18}	– – –	4.56×10^{-19}	7.56×10^{-18}
Specific gravity	1.143–1.207	– – –	1.110–1.196	1.028–1.031	1.028–1.029
Refractive index (20°C)	1.5210–1.5272	1.5228	1.520	1.5248	1.4976
Coefficient of refractive index	0.000112–0.00021 (20–40°C)	0.000200 (20–30°C)	– – –	0.000167 (20–50°C)	0.000400 (20–90°C)
Molar refraction	– – –	– – –	– – –	495	137
Energy of activation, viscous flow					
E_0 of molten lac, kcal.	28.74	38.13	– – –	31.61–33.34	25.32–47.67
Molar axial ratio[c]	– – –	10.3	– – –	11.3	7.8
Magnetic susceptibility, emu	-0.30×10^{-6}	– – –	– – –	– – –	– – –
Dipole moment, D	– – –	– – –	– – –	7.45	4.61
Sound transmission, 20°C, m/sec	– – –	– – –	970	– – –	– – –
Specific rotation, $[\alpha]_D^{25}$,°	– – –	+60.71	+59.29	+54.83	+63.60
Acid value	65–75	69–71	73–118	55–60	103–110
Saponification value	220–230	225–230	176–276	218–225	207–229
Hydroxyl number	250–280	230–264	232–248	235–240	116–117
Iodine value, methods					
Wijs (1 h)	14–18	– – –	10–11	11–13	50–55
Hydrogen absorption	23–25	18–19	– – –	13–16	50–60
Carbonyl value					
Sulfite method	7.8–27.5	18.0–20.0	– – –	17.6	17.3

[a]Table from Misra and Sengupta[3]: Listing of properties rearranged; MW by osmometric method[14] inserted.
[b]Volume of moving unit during flow; since viscous volume is greater than the molecular volume, the material appears to take the form of aggregates.
[c]Ratio of length to breadth of dissolved units.

USE

Cosmetic Uses

"Bleached, dewaxed Shellac in the form of brittle, yellowish transparent sheets or crushed pieces is commercially used by the cosmetic industry."[7] It is prepared by high temperature dissolution of seedlac in an alkaline aqueous solution. Purification and dewaxing accomplished by centrifugation or filtration are followed by bleaching with dilute sodium hypochlorite. The Bleached Dewaxed Shellac is precipitated from the hypochlorite solution with a dilute mineral acid. Further purification of Shellac includes filtration, washing, and drying.[7]

Current cosmetic product formulation data listing ingredients and their concentration ranges in particular product type categories are obtained from the Food and Drug Administration.[21] Cosmetic manufacturers and formulators voluntarily file these data with the FDA in accordance with Title 21 Section 720.4 of the Code of Federal Regulations.

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. 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 two- to ten-fold error in the assumed ingredient concentration.

FDA's most recent product formulation data table in 1983 lists Shellac in a total of 77 reported formulations.[21] Eight of the 77 items reported were in categories containing formulation data for less than or equal to 5 products. According to the FDA, these voluntary formulations were excluded from the final printout for proprietary reasons. The remaining 69 formulations appeared in the following product categories: eyeliner, mascara, and hair sprays (Table 5).

The range of Shellac concentration in mascara was 0.1 to 25%. The concentration of Shellac in eyeliners ranged from 1 to 10%. All 6 of the reported hair spray formulations contain Shellac in concentrations from 0.1 to 1%.

TABLE 5. Product Formulation Data on Shellac[21]

Product category	*Total no. of formulations in category*	*Total no. containing ingredient*	*No. of product formulations within each concentration range (%)*			
			>10–25	*>5–10*	*>1–5*	*>0.1–1*
Eyeliner	382	21	–	10	11	–
Mascara	429	42	12	11	19	–
Hair sprays (aerosol fixatives)	285	6	–	–	–	6
1983 TOTALS		69	12	21	30	6

Noncosmetic Use

Food

The safety of Shellac used as a direct food additive is currently under evaluation by the FDA.

Federal regulations allow Shellac as an indirect food additive when used as a component of adhesives intended for packaging, transporting, or holding food (21 CFR 175.105[c][5]).[22] Shellac may also be used as an indirect food additive in the resinous and polymeric coating of food-contact surfaces intended for use in producing, manufacturing, packaging, transporting, or holding food (21 CFR 175.300[b][3][iv])[22] (natural fossil resins, as the basic resin: Shellac); and in the food-contact surface of paper and paperboard (21 CFR 176.170[a][4]).[22] Food-grade Shellac may also be used with no restrictions as a diluent in color additive mixtures for marking food; specifically in inks for marking food supplements in tablet form, gum, and confectionery (21 CFR 73.1[b][1][i]).[22]

Other Uses

Nonfood uses for Shellac include its use as a high-grade wood finish and undercoat sealer, metal surface anticorrosive etch primer, mirror sealer, printing ink vehicle, leather dressing, floor polish, paper glaze, photoengraving material, electrical insulator, rubber additive, cement component, and varnish for munitions.[19]

BIOLOGICAL PROPERTIES

Pharmaceutical glazes containing 20.0–51.0% anhydrous Shellac in alcohol[20] were introduced to "resist the action of gastric fluids" in passage of coated tablets through the stomach for ultimate drug absorption in the small intestine.[23] These coatings were expected to "disintegrate" and "dissolve" by the time they reached the small intestine.[23] The major constituents in these coatings include fatty acids, waxes, and cellulose acetate phthalates (CAP) as well as Shellac.[23] The ester bonds of the lac resin polymer can easily by hydrolyzed by gastric acidity[23] and/or intestinal esterases.[24] These esterases and other hydrolytic enzymes have also been found in the plasma and body tissues.[23] Variable degrees of hydrolysis may occur in any one of these compartments, since the time for passage of enteric-coated tablet past the pylorus has ranged from a few to 12 h among individuals.[23] Lee et al.[25] noted a significant individual variation among six subjects in the dissolution rate of Shellac-coated tablets of prednisolone when compared with CAP-coated ones. Data in this study indicated that the Shellac coating did not appreciably disintegrate within the digestive tract.

TOXICOLOGY

Acute Oral Toxicity

The acute oral toxicity of five types of food-grade Shellac was determined in rats.[26] The types of Shellac included Regular Bleached Bone-Dry Shellac, Refined Wax-Free Bone Dry Bleached Shellac, Orange Wax-Containing Shellac,

Orange Wax-Free Shellac and Shellac Wax (see Fig. 1). Ten rats per group within the weight range 200 to 300 g were fed one 5 g/kg dose of one type of Shellac in aqueous suspension. No deaths were recorded.

A cosmetic product, Mascara X (mascara emulsion with film formers), containing 5% Shellac was fed to 10 Sprague-Dawley strain albino rats at a dose of 10 ml/kg body weight.[27] The rats appeared normal after dosing and during the 14-day observation period; body weights increased, and no abnormalities of the thoracic or abdominal organs were found at necropsy.

Mascara Y, containing 6% Shellac, was fed to 10 young adult Sprague-Dawley rats in a 50% aqueous solution at a maximum practical dose (MPD) of 20 g/kg.[28] The MPD was considered "practically nontoxic" based on three criteria: nonlethality (all 10 animals survived), no overt toxic responses (other than mild sedation or irritability) throughout the test period, and no compound-induced alterations at necropsy.

Reproduction and Subchronic Oral Toxicity

A reproduction and subchronic feeding study in Sprague-Dawley rats used Regular Bleached Shellac at concentartions of 0 (control), 1000, 3000, and 10,000 ppm mixed in a commercial feed.[29] Each group of male and female rats (F_0; 25 per sex) was fed for 28 consecutive days; animals within respective groups were mated after this period, and a single litter (F_1) was delivered. Twenty-five weaned F_1 animals from each group were then fed with the same F_0 diets for an additional 90 days. Animals were evaluated and data were collected on mortality, external physical/behavioral/developmental signs of toxicity, body weight, feed consumption, reproduction and lactation, hematology, clinical chemistry, urine analysis, and gross and microscopic alterations. The investigators concluded that there was no evidence of treatment-related toxic or pathological effects in Shellac-fed F_0 or F_1 animals and fertility, reproductive performance, and pup development were similar at all concentrations of Shellac feeding.

Skin Irritation

Mascara Y (6% Shellac concentration) was assessed for skin irritation.[30] Doses of 0.5 g Mascara Y were applied to clipped dorsal and lateral areas of 6 female NZW rabbits at 24-h intervals for a total of three applications. After a 6-h exposure time, excess material was gently removed with mild soap and water, and the exposure site was evaluated for primary irritation.[31] This process was repeated, exposing the same site the following 2 days after 24-h nontreatment periods. Very slight erythema was found in one of the six rabbits after 24 h (Day 1), in two rabbits after 48 h (Day 2), and in three rabbits after 72 h (Day 3). No other responses were observed (Table 6).

Mascara X was evaluated for skin irritation by placing 0.5 ml of the 5% Shellac-containing mascara on both unabraded and abraded abdominal skin of six male albino rabbits using an occlusive patch technique.[27] Two rabbits had very slight erythema (value = 1, range of 0–4) at abraded sites after 24 h, but the sites were normal when examined after 72 h. Each of the two rabbits had individual

TABLE 6. Animal Toxicity Testing

Ingredient	*Animal*	*Method*	*Results*	*Reference*
		DERMAL		
Shellac, 6% in Mascara Y	6 rabbits, NZW	Draize Primary Dermal Irritation Test 0.5 g Mascara Y	1/6 very slight erythema at 24 h 2/6 very slight erythema at 48 h 3/6 very slight erythema at 72 h No other abnormal responses	30
Shellac, 5% in Mascara X	6 rabbits, albino	Primary Dermal Irritation 0.5 ml Mascara X 24-h occlusive patch on abraded and unabraded abdominal skin	2/6 very slight erythema (1 on scale of 0–4) abraded site, 24 h No erythema at 72 h No edema in any animal Mean PII = 0.083 (range 0–8)	27
Shellac, 5% in Mascara X	6 rabbits, NZW	Acute Dermal Toxicity approx. 10 g/kg body weight Mascara X 24-h occlusive patch on shaven trunk	No deaths, LD_{50} > 10 g/kg body weight No abnormal dermal, weight, or behavior response Gross autopsy results not reported	27
		OCULAR		
Shellac, 5% in Mascara X	6 rabbits	Draize Eye Irritation Test Eyes not rinsed after treatment. 100 μl Mascara X	5/6 slight conjunctival erythema (1 on scale of 0–3) at 24 h 3/6 slight conjunctival erythema (score 1) at 48 h All animals appeared normal after 72 h	27
Shellac, 6% in Mascara Y	9 rabbits, NZW	Draize Test 6/9 eyes unrinsed 3/9 eyes rinsed	1/6 in unrinsed group had conjunctival erythema (score not reported) which cleared after 96 h No other abnormal responses	32

PIIs of 0.25. The mean PII for all animals of this study was 0.083, well below the empirically set PII of 5 or more (PII ≥ 5) for primary skin irritants (PII range 0–8) (Table 6).

Acute Dermal Toxicity

Mascara X was tested for acute dermal toxicity at a dose of 10 g/kg body weight in six young adult New Zealand albino rabbits. The trunks of six rabbits were shaved 24 h before sample application to allow recovery of the stratum corneum. Mascara X was applied under a plastic sheeting sleeve at a "maximum practical volume up to run-off."[27] After a 24-h contact time, the plastic sleeve and any excess test material were removed. All six rabbits survived the dose and appeared normal immediately after dosing and during the 14-day observation period. The acute dermal LD_{50} was greater than 10 g/kg body weight (Table 6).

Ocular Irritation

Mascara X was tested for ocular irritation by instilling 100 μl into the right eyes of six rabbits.[27,33] The cornea and iris of treated eyes of all animals appeared normal. However, five of the six rabbits had slight conjunctival erythema (score of 1 in range of 0–3) after 24 h. Three had slight redness after 48 h, and none of the animals had any toxic response after 72 h.[34] Except for these slight and reversible reactions, none of the animals had a completely "positive" reaction (16 CFR 1500.42)[22] (Table 6).

Acute ocular irritation of Mascara Y (6% Shellac) was evaluated in nine young adult female NZW rabbits[32] using the Draize Eye Irritation Test (Draize, 1959). The nine animals in the two groups were treated in the following manner: 100 mg Mascara Y was instilled into the conjunctival sacs of the six rabbits in the first group; the three rabbits in the second group had the same treatment, but it was followed four seconds later by an isotonic saline rinse. Eight of the nine animals had no positive response to Mascara Y throughout the experiment. One rabbit in the first group had conjunctival erythema that had cleared by 96 h. No other toxic effects were observed (Table 6).

Respiratory Toxicity

Samples of six major types of aerosol hair sprays used in 1959 were selected for studies of acute and subchronic toxicity because of the possibility of inhalation of solid, nonvolatile residues by users of these formulations.[35] Natural and synthetic resin components in the formulations were considered the sources of this residue. One of the six hair sprays tested contained Shellac.

A total of 30 rabbits, 5 per spray type, were partially immobilized in an exposure box and fitted with protective eye goggles. Sample spray was directed 6–12 inches from the back and sides of the animals' heads. The acute inhalation toxicity test consisted of 30-second spray releases every half-hour until the contents of the container were completely used (275–400 g range in total weight of contents). Each 30-second spraying accounted for 20–35 g (mean, 30 g) of spray. No adverse effects were observed during the acute exposure period or during the following 4 days. No gross or microscopic lesions were found in the respiratory tracts or in associated lymphoid structures.

The chronic inhalation study of Draize et al.[35] consisted of daily AM and PM exposures of rabbits (five per spray type) to 30-second spray releases for a period of 90 days. Animals remained in the exposure chamber 15 minutes. No adverse effects were observed during or at completion of the 90-day exposure period. Radiographs taken after 90 days were compared to prestudy radiographs, and no alterations or radiopaque matter retention by the lungs was found. No abnormalities were observed in hemograms obtained either during or following the 90-day exposure period. No lesions different from those in control animals were found in treated animals at necropsy.

Mutagenicity

Shellac wax in the form of hard-surfaced chunks suspended in 10% dimethylsulfoxide (DMSO) was evaluated for mutagenic activity in microbial assays with *Saccharomyces cerevisiae*, strain D4, and *Salmonella typhimurium*, strains TA1535, TA1537, and TA1538.[36] Metabolic activation preparations were 9000 *g* supernatants obtained from homogenates of the lungs, liver, and testes from random-bred adult male ICR mice, Sprague-Dawley adult male rats, and adult male *Macaca mulatta*. Shellac Wax concentrations of 0.015% and 0.03% in *S. typhimurium* cultures and 0.25% and 0.5% in *S. cerevisiae* cultures with and without metabolic activation had no significant genotoxic activity.

A "mutagenicity evaluation of regular bleached food-grade Shellac using the Ames Salmonella/Microsome Plate Test" was performed on eight concentrations ranging from 1 to 10,000 μg/plate Shellac in corn oil.[37] A series of in vitro microbial plate assays were performed using *S. typhimurium* strains TA1535, TA1537, TA1538, TA98, and TA100 in the absence and in the presence of S9 fraction from Aroclor-induced rats. The negative control for both activation and nonactivation assays consisted of incubation of the strains with corn oil alone. In the nonactivation assays, the positive control for strains TA1535 and TA100 was sodium azide in water at a concentation of 10.0 μg/plate, that for TA1538 and TA98 assays was 10.0 μg/plate 2-nitrofluorene in DMSO, and that for TA1537 assays was 50.0 μg/plate 9-aminoacridine in ethanol. The positive control, 2-anthramine in DMSO at a concentration of 2.5 μg/plate, was used in the activation assays with all five strains. No toxicity was observed in any of the indicator strains used. No increase in the number of revertants was observed in any strain either in the presence or in the absence of metabolic activation.

CLINICAL ASSESSMENT OF SAFETY

Irritation/Sensitization

Mascara X, containing 5% Shellac, was tested for irritation and sensitization using repeated insult patch procedures using 102 human subjects.[38] An induction phase consisted of applications of 10 occlusive patches for 48 h to the backs of subjects and scoring for irritation, with the removal of each patch followed by an 11-day nontreatment period. An occlusive challenge patch was then applied to fresh sites and scored 15 minutes and 24 h after removal following the 48-h challenge period. Twelve of the original 105 subjects were absent for one or more of the induction patches; 3 of these 12 did not complete the study. Of the 102 subjects completing the study, 2 had erythema without edema: the first had a single reaction after the tenth induction patch, and the second had a single reaction after the fourth induction patch. Two other subjects had slightly positive reactions. None of the 102 subjects had positive sensitization reactions to the challenge patches (Table 7).

A modified Draize-Shelanski-Jordan repeated insult patch test (RIPT) was used to test Mascara Y (6.0% Shellac) for dermal sensitization using 205 subjects.[39] An induction phase consisting of nine 48-h applications (site evaluation for irritation after removal of each patch) was followed by a 2-week nontreatment period. Subjects were then challenged at fresh sites by 48-h and 98-h

TABLE 7. Clinical Assessment of Safety Irritation/Sensitization and Photosensitization Studies

Ingredient	*No. of humans*	*Method*	*Results/Comments*	*Reference*
		IRRITATION/SENSITIZATION		
Shellac, 5% in Mascara X (unreported dose)	102	RIPT[a]	2/102 erythema, no edema 2/102 doubtful reactions No positive sensitization reactions to challenge patches	38
Shellac, 6% in Mascara Y (unreported dose)	205	Modified Draize-Shelanski-Jordan RIPT	1/205 1+ reaction No reactions at challenge	39
Shellac, 6% in Mascara Y	27	28-day controlled use test	No complaints of any adverse reactions	40
Shellac, 5.88% in Mascara Z (unreported dose)	205	Modified Draize-Shelanski RIPT	No adverse induction or challenge reactions	41
		PHOTOSENSITIZATION		
Shellac, 6% in Mascara Y (100 μl/cm^2)	23	Xe source, λ range 290–400 nm. 3 MED irradiation after 24-h occlusive patch; 6 exposures; 10-day rest; 24-h occlusive challenge at fresh site; 3 min UVA irradiation	No adverse induction or challenge reactions	42

[a]Repeated Insult Patch Test.

applications of the test material. One of the 205 subjects had a 1+ reaction on induction, a response of faint, macular erythema of at least 25% of the test area. No other reactions after induction or challenge patches were recorded (Table 7).

Mascara Y was also evaluated in a controlled-use test involving 27 human subjects. The test product was used as directed daily for 28 days. Subjects were instructed to discontinue the use of similar product(s) during the evaluation period. No adverse reactions were recorded[40] (Table 7).

The third Shellac product, Mascara Z, containing 5.88% Shellac, was evaluated for irritation and/or sensitization in a modified Draize-Shelanski RIPT using 205 subjects.[41] No adverse induction or challenge reactions were observed (Table 7).

Photosensitization

One study of human photosensitization used a Shellac product, Mascara Y (6.0% Shellac), at a dose of 100 μl/cm^2 and 23 subjects.[42] A xenon light source that emits light within the wavelength spectrum of 290–400 nm was used. After estimating the minimal erythema dose (MED) for each individual[43] at one site (site 1), Mascara Y was applied to a fresh site (site 2) under an occlusive alumi-

num patch. After 24 h, this patch was removed, and site 2 was evaluated for irritation and then irradiated with three times the MED. These sites were evaluated again after 48 h, and new occlusive patches were applied. The procedure was repeated twice weekly for a total of six exposures, followed by a 10-day nontreatment period. A challenge dose at a fresh site (site 3) under an occlusive dressing was then applied. At 24 h, on removal of this patch, site 3 was evaluated for irritation and then irradiated for 3 minutes using the Xe source with a Schott WG345 filter that excluded UVB radiation in the wavelength range of 280–320 nm. Scoring of site 3 was done at 15 minutes, 24 h, 48 h, and 72 h after irradiation. The controls included an evaluation of the response to Mascara Y with no irradiation and an evaluation of the response to irradiation with no Mascara Y exposure. Since no reaction was observed in any of the 23 subjects, Mascara Y was neither phototoxic nor photoallergenic under these test conditions (Table 7).

Respiratory Studies

In 1963, Gelfand suggested that the respiratory allergies associated with Shellac inhalation in the "beauty culture industry" were not due to Shellac but to the solvents in hair sprays. These solvents were the amines, ethylene diamine and hexamethylene tetramine.[44]

The possible association between the inhalation of resins in hair sprays and a chronic respiratory disease, "pulmonary thesaurosis," has been reviewed.[45]

In conjunction with the acute and subchronic rabbit inhalation toxicity studies, Draize et al.[35] conducted a preliminary study with an unreported number of women volunteers. One of the six hair spray formulations contained Shellac. A mean spray-release time of 10 seconds was determined during normal hair spraying operation at a distance indicated in label directions on the containers. If no directions were available, the container was held at a distance of 6 inches for half the spray-release time and at 12 inches for the remaining half. Each subject was exposed to a 10-second and an empirical exaggerated 30-second release of spray. Solid particle intake from various sprays was calculated using differential weight measurement of a sampling tube placed 1 foot in front of each subject's mouth at t_0 and t_f = 5 or 10 minutes (where t_0 = initial time before spraying; t_f = final time, after 5 or 10 minutes of spraying). Results for all sprays tested were expressed as the average for all six sample types. About 65% of the weight of released unimpinged hair spray was made up of particles in the range of 10 μm or less in diameter, indicating that a significant portion of total material released was in a size range that could have reached the alveoli. Minimal quantities of dry spray collected by the sampling tube from 1 cubic foot of air were available for inspiration following either the 10-second spray-release (30–40 μg) or 30-second spray-release (200 μg–2.0 mg), indicating that a large percentage of particles were impinged on the hair or settled rapidly from the atmosphere after release. These amounts were considered insufficient to produce adverse effects.[35]

SUMMARY

Lac is the hardened resinous secretion of a tiny-scale insect, *Kerria lacca* (Fam. Coccidae). Bleached, dewaxed Shellac is commercially used by the cosmetic industry.

Cosmetic-grade Shellac is a mixture of hydroxyaliphatic and alicyclic acids and their polyesters. The composition of the mixture varies with the lac source and the time of collection. The major component of the aliphatic fraction is aleuritic acid. The alicyclic fraction consists of sesquiterpenic acids, primarily jalaric acid and its derivatives. The lac resin is thought to be a 2095 ± 110 MW polymer of four jalaric acid molecules alternating with four aleuritic acid molecules in ester linkage.

The cosmetic industry uses Shellac dissolved in alcohol or in alkaline aqueous solutions primarily for mascara, hair spray, and eyeliner product formulations. FDA product formulation data reported in 1983 indicated that 77 formulations contained Shellac, 69 of which were listed in the three major product categories. The 1981 data tables contained 76 formulations and included the minor product categories. The concentration range was 0.1 to 25% in 1983, and the lowest range was reported for hair sprays (0.1–1%). Shellac concentrations in eyeliner ranged from 1 to 10% and in mascara, the range was 1 to 25%.

Shellac is also widely used by the pharmaceutical and confectionery industry for tablet and candy coatings, respectively. It is a class 5 GRAS substance pending possible reclassification to class 1 based on FDA evaluation of a requested chronic feeding study.

Cosmetic-grade Shellac had an LD_{50} of greater than 5 g/kg in rats. Results of acute animal toxicity studies using cosmetic formulations containing up to 6% Shellac indicated no adverse effects upon oral (rats), dermal (rabbits), ocular (rabbits), and respiratory tract (rabbits) exposure. Chronic inhalation of a Shellac hairspray formulation by rabbits produced no toxicity. No treatment-related toxic or pathological effects were observed when concentrations of up to 10,000 ppm Regular Bleached Shellac were fed to rats in a subchronic study.

Mutagenicity assays using *Saccharomyces cerevisiae* strain D4 (Shellac wax) and *Salmonella typhimurium* histidine auxotrophs TA1535, TA1537, TA1538, TA98, TA100 (Shellac and Shellac Wax) with and without metabolic activation were negative.

Clinical assessment of the safety of Shellac cosmetic formulations containing up to 6% Shellac indicated no measurable irritation and absence of sensitization and photosensitization.

DISCUSSION

The Panel's conclusion is limited to the refined wax-free bleached or cosmetic-grade Shellac. Further the Panel noted that most of the data were on product formulations and limited the conclusion to the maximum concentration tested, 6%.

CONCLUSION

Based on the animal and clinical data included in this report, the CIR Expert Panel concludes that cosmetic-grade Shellac is safe for use in cosmetic formulations at concentrations up to 6%.

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