Final Report of the Cosmetic Ingredient Review Expert Panel

Safety Assessment of Simmondsia Chinensis (Jojoba) Seed Oil, Simmondsia Chinensis (Jojoba) Seed Wax, Hydrogenated Jojoba Oil, Hydrolyzed Jojoba Esters, Isomerized Jojoba Oil, Jojoba Esters, Simmondsia Chinensis (Jojoba) Butter, Jojoba Alcohol, and Synthetic Jojoba Oil

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Cosmetic Ingredient Review

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Final Report on the Safety Assessment of Simmondsia Chinensis (Jojoba) Seed Oil, Simmondsia Chinensis (Jojoba) Seed Wax, Hydrogenated Jojoba Oil, Hydrolyzed Jojoba Esters, Isomerized Jojoba Oil, Jojoba Esters, Simmondsia Chinensis (Jojoba) Butter, Jojoba Alcohol, and Synthetic Jojoba Oil

ABSTRACT: Several cosmetic ingriedients derive from the desert shrub *Simmondsia chinensis*, including Simmondsia Chinensis (Jojoba) Seed Oil, Simmondsia Chinensis (Jojoba) Seed, and Simmondsia Chinensis (Jojoba) Butter. Further processing produces other ingredients including Hydrogenated Jojoba Oil, Hydrolyzed Jojoba Esters, Isomerized Jojoba Oil, Jojoba Esters, and Jojoba Alcohol. Synthetic Jojoba Oil also is used in cosmetics. In this group Simmondsia Chinensis (Jojoba) Seed Oil, the most widely used ingredient, and safe at concentrations up to 100% in body and hand creams, is expressed from seeds and is composed almost completely (97%) of wax esters of monounsaturated, straight-chain fatty acids and alcohols with high-molecular weights. Amounts and composition of the expressed oil varies with maturity of the seeds and somewhat with plant location and climate. Plant derived material may also contain pesticide residues and/or heavy metals. Most available safety test data examined the expressed oil. For example Simmondsia Chinensis (Jojoba) Seed Oil was reported to readily penetrate nude mouse skin and to increase penetration of other agents such as aminophylline in clinical tests. Simmondsia Chinensis (Jojoba) Seed Oil was not an acute oral toxicant to mice or rats (LD_{50} generally greater than 5.0 g/kg). Short-term subcutaneous administration of Simmondsia Chinensis (Jojoba) Seed Wax to rats at 1 ml/kg was not toxic. Neither the wax nor the oil were toxic when applied dermally to the shaved backs of guinea pigs in short-term tests. A dermal irritation test found aqueous Hydrolyzed Jojoba Esters (20%) to be non-irritating to guinea pigs. Jojoba Alcohol was found to be non-irritating to the skin of albino marmots at 10.0%. Simmondisa Chinensis (Jojoba) Butter was classified as a non-irritant when applied to the intact and abraded skin of New Zealand white rabbits at 0.5 ml for 24 h under an occluded patch. Jojoba Alcohol at concentrations up to 50% was minimally irritating in rabbits. Simmondsia Chinensis (Jojoba) Seed Oil was non- to slightly irritating when instilled into the eyes of white rabbits, but Simmondsia Chinensis (Jojoba) Seed Wax, Jojoba Esters, and Jojoba Alcohol were not. Simmondsia Chinensis (Jojoba) Seed Wax was moderately comedogenic in tests using rabbits, but Jojoba Esters was noncomedogenic, and Jojoba Esters were non- to slightly- comedogenic. Simmondsia Chinensis (Jojoba) Butter, Jojoba Alcohol, and Jojoba Esters were non-mutagenic in Ames testing. No carcinogenicity and no reproductive or developmental toxicity data were available. In clinical tests, Simmondsia Chinensis (Jojoba) Seed Oil was neither a significant dermal irritant, nor a sensitizer. In repeat insult patch tests Jojoba Alcohol , Jojoba Esters and Hydrolyzed Jojoba Esters were not irritating during induction or sensitizing at challenge. Simmondsia Chinensis (Jojoba) Seed Oil and Jojoba Alcohol were not phototoxic. The available safety test data were combined with the expected uses of these ingredients, which includes use in aerosolized products. Because the particle size of aerosol hair sprays (~38 μm) and pump hair sprays (>80 μm) is large compared to respirable particulate sizes (≤10 μm), the ingredient particle size is cosmetic aerosols is not respirable. Relevant information also included uses with baby and eye products at low concentrations, and at 100% in hand and body creams. There were no structural alerts for the fatty acids, fatty alcohols, or other structures that would be found in these ingredients relative to reproductive/developmental toxicity, and these ingredients are not expected to easily penetrate skin. None of the tested ingredients were genotoxic and there were no structural alerts for carcinogenicity. The cosmetic industry should continue to limit pesticide and heavy metal impurities in the plant-derived ingredients before blending into cosmetic formulations. The CIR Expert Panel recognizes the gaps in use and use concentration data of these ingredients. Generally, the information available on the product types that include these ingredients and at what concentrations indicate a pattern to the Expert Panel when it assessed ingredient safety. Were unused ingredients used in the future, use is expected in comparable product categories and concentrations.

INTRODUCTION

Simmondsia Chinensis (Jojoba) Seed Oil and Simmondsia Chinensis (Jojoba) Seed Wax were previously reviewed by the Cosmetic Ingredient Review (CIR) Expert Panel and were found to be "...safe as cosmetic ingredients in the present practices of use and concentration" (Elder 1992). In the original safety assessment, the name of Simmondsia Chinensis (Jojoba) Seed Oil was Jojoba Oil and the name of Simmondsia Chinensis (Jojoba) Seed Wax was Jojoba Wax. The original safety assessment also considered data relevant to the safety of Jojoba-derived ingredients in addition to the oil and wax. Newly available published and unpublished data on all Jojoba-derived ingredients have been included in this report. Accordingly, this amended safety assessment includes Simmondsia Chinensis (Jojoba) Seed Oil, Simmondsia Chinensis (Jojoba) Seed Wax, Hydrogenated Jojoba Oil, Hydrolyzed Jojoba Esters, Isomerized Jojoba Oil, Jojoba Esters, Simmondsia Chinensis (Jojoba) Butter, Jojoba Alcohol, and Synthetic Jojoba Oil.

CHEMISTRY

Definition and Structure

Simmondsia Chinensis (Jojoba) Seed Oil (CAS No. 61789-91-1) is defined as the fixed oil expressed or extracted from seeds of the desert shrub, Jojoba, *Simmondsia chinensis*. It is also known as Buxus Chinenesis Oil, Jojoba Oil, and Jojoba Seed Oil. Its chemical classification is ester. It only has plant sources

(Gottschalck and Bailey 2008).

According to Wendel (1980), the following chemical formula is typical of an ester found in Jojoba Oil.

$$CH_3(CH_2)_7CH=CH\text{-}(CH_2)_7CO\text{-}O\text{-}(CH_2)_{11}CH=CH(CH_2)_7CH_3$$

Simmondsia Chinensis (Jojoba) Seed Wax (CAS No. 61789-91-1, same as the oil) is defined as the wax obtained from the seed of the jojoba plant, *S. chinensis*. Its chemical classification is wax, and it comes from plant sources (Gottschalck and Bailey 2008).

Hydrogenated Jojoba Oil (no CAS No.) is defined as the end product of the controlled hydrogenation of Simmondsia Chinensis (Jojoba) Oil. Its chemical classification is wax. It has both plant and synthetic sources (Gottschalck and Bailey 2008). According to the *International Cosmetic Ingredient Dictionary and Handbook*, a synthetic source is assigned to an ingredient that is prepared ("synthesized") by the reaction of a substance with one or more other substances to form a new chemical entity. In cases when it is very clear that a raw material used to synthesize an ingredient is plant or animal derived, that source may be listed (Gottschalck and Bailey 2008).

Hydrolyzed Jojoba Esters (no CAS No.) is defined as the hydrolysate of Jojoba Esters (q.v.) derived by acid, enzyme, or other method of hydrolysis. Its chemical classification is esters. It has only a plant source (Gottschalck and Bailey 2008).

Isomerized Jojoba Oil (no CAS No.) is defined as a mixture of esters produced by the enzymatic intraesterification of Simmondsia Chinensis (Jojoba) Oil (q.v.). Its chemical classification is ester. It has both plant and synthetic sources (Gottschalck and Bailey 2008).

Jojoba Esters (no CAS No.) is defined as a complex mixture of esters produced by the transesterification/ interesterification of Simmondsia Chinensis (Jojoba) Oil (q.v.), Hydrogenated Jojoba Oil (q.v.), or a mixture of the 2. Its chemical classifications are transesters and waxes. It has both plant and synthetic sources (Gottschalck and Bailey 2008).

Simmondsia Chinensis (Jojoba) Butter (no CAS No.) is defined as the material obtained by the isomerization of Simmondsia Chinensis (Jojoba) Oil (q.v.). Its chemical classification is wax (natural and sythethic). It has only plant sources (Gottschalck and Bailey 2008).

Jojoba Alcohol (no CAS No.) is defined as the alcohol fraction obtained by the saponification of Simmondsia Chinensis (Jojoba) Oil (q.v.). Its chemical classification is fatty alcohols. It has only plant sources (Gottschalck and Bailey 2008).

Synthetic Jojoba Oil (no CAS No.) is defined as a synthetic oil intended to be generally indistinguishable from natural jojoba oil with regard to chemical composition and physical characteristics. Its chemical classification is wax and it only has synthetic sources (Gottschalck and Bailey 2008).

Physical and Chemical Properties

Simmondsia Chinensis (Jojoba) Seed Oil

The reaction of Simmondsia Chinensis (Jojoba) Seed Oil with sulfur yields a stable product; the liquidity of the oil is not affected by this reaction. Simmondsia Chinensis (Jojoba) Seed Oil also readily undergoes hydrogenation in the presence of a variety of nickel catalysts. The crystalline, hydrogenated product formed has a melting point of approximately 70°C. The epoxidation of Simmondsia Chinensis (Jojoba) Seed Oil and the amidation of transesterified Simmondsia Chinensis (Jojoba) Seed Oil have also been reported. Simmondsia Chinensis (Jojoba) Seed Oil is not easily oxidized and remains chemically unchanged for years. It also remains essentially unchanged when heated repeatedly to temperatures above 285°C, or after being heated to 370°C for 4 days. The yellow color of Simmondsia Chinensis (Jojoba) Seed Oil disappears permanently when the oil is heated to 300°C over a short period of time (McKeown 1983).

Rheological analysis of Simmondsia Chinensis (Jojoba) Seed Oil gave a viscosity of 37.7 mPa/s (Esquisabel et al 1997).

Chung et al. (2001) reported that Simmondsia Chinensis (Jojoba) Seed Oil formed stable emulsions in water with small particles (225 nm; polydispersity 0.21; viscosity 43.0 cSt/s).

Esquisabel et al. (2002) reported that the emulsion of Simmondsia Chinensis (Jojoba) Seed Oil and water encapsulating Bacillus Calmette-Guérin were stable after freeze-drying and storage at room temperature for a year.

Properties of what Habashy et al. (2005) referred to as "jojoba liquid wax", thought to be Simmondisa Chinenesis (Jojoba) Seed Oil, are listed in Table 1.

Table 1. Physical properties of jojoba liquid wax (Habashy et al. 2005).

Property	Value
Freezing point	9°C
Boiling point	398°C
Smoke point[a]	195°C
Flash point	295°C
Refractive index at 25°C	1.46
Specific gravity at 15°C	0.87
Viscosity (25°C)	50 cP
Iodine value	81
Saponification value	93
Acid value	2
Acetyl value	2
Unsaponifiable matter	51%
Total acids	52%

[a] Determined according to official method, Cc9a-48, of the American Oil Chemists' Society

Simmondsia Chinensis (Jojoba) Seed Wax

Kampf et al. (1986) reported that crude Simmondsia Chinensis (Jojoba) Seed Wax has an initial peroxide value of 17 meq/kg, and reaches almost zero after stripping or bleaching. The induction time was 45 to 50 h for crude wax, 12 h for bleached, and 2 h for stripped. Freshly bleached Simmondsia Chinensis (Jojoba) Seed Wax had a low peroxide value of 0 to 0.5 meq/kg for several months when stored in the dark at room temperature; the value elevated to 70 meq/kg within 6 to 7 weeks when stored in a transparent glass bottle. The authors suggest that crude Simmondsia Chinensis (Jojoba) Seed Wax contains a natural antioxidant that is lost in the bleaching and stripping processes.

Simmondsia Chinensis (Jojoba) Seed Wax is a hard crystalline material with properties that are comparable to carnauba and beeswax, and it is miscible with polyethylene glycol in all proportions. The properties of Simmondsia Chinensis (Jojoba) Seed Wax are as follows: appearance of white to off-white free flowing hard wax flakes, slight fatty odor, saponification number of 90 to 95, iodine value of 1, and melting point of 69°C (Reinhardt and Brown 1990).

Jojoba Esters

The physical consistency of Jojoba Esters ranges from a semisolid paste to a liquid with properties that are almost identical to those of Simmondsia Chinensis (Jojoba) Oil. The properties of 2 Jojoba Esters are as follows: soft white to off-white appearance, typical fatty odor, saponification number of 90, iodine values of 60 and 40, and melting points of 29 and 58°C (Reinhardt and Brown 1990).

Brown et al. (1997) tested the stability of Jojoba Esters 15 (melting point 15°C) and Jojoba Esters 60 (melting point 60°C) using an oxidative stability index (OSI; also referred to oil stability index) using a method developed by the American Oil Chemists' Society (AOCS 1997). Jojoba Esters 15 had a stability of ~35 OSI hours and Jojoba Esters 60 175 OSI hours. For comparison, the stability of sesame oil was ~15 OSI hours, palm oil ~30 OSI hours, macademia oil ~30 OSI hours, hybrid sunflower oil ~35 OSI hours, traditional sunflower oil ~5 OSI hours, and almond oil ~10 OSI hours. Table 2 shows the OSI for the Jojoba Esters when exposed to cosmetic actives.

The melting point of Jojoba Esters-70 is 70°C (Arquette et al. 1998).Jojoba Esters have melting points ranging from 15°C to 70°C. The texture and crystallinity of Jojoba Esters may be modified by rapid cooling, thus altering their properties. Jojoba Esters are resistant to oxidation (International Jojoba Export Council 2004).

Floratech (2005a,b,c) reported on 5 Jojoba Ester products (see COMPOSITION SECTION). The properties are reported in Table 3. The shelf life of all 5 Jojoba Esters in an unopened container at or below 35°C is 1 year.

Table 2. OSI of Jojoba Esters 15 and 60 when exposed to cosmetic actives (Brown et al. 1997).

Cosmetic active (%)	15 h	60 h
None	~35	~175
Tocopherols*	~80	~230
Iron oxides (10%) and tocopherols	~80	~225
Zinc oxides (10%) and tocopherols	~15	~90
Titanium dioxide (10%) and tocopherols	~135	~300
Malic acid (5%) and tocopherols	~110	~20
Salicylic acid (2%) and tocopherols	~25	~50
Salicylic acid (2%), titanium dioxide (10%), and tocopherols	~60	~180
Malic acid (5%), titanium dioxide (10%), and tocopherols	~120	~20
Arbutin (7%) and tocopherols	~50	~90
Kojic acid (1%) and tocopherols	~100	~250
Magnesium ascorbyl phosphate (3%) and tocopherols	~85	~170

* concentration of tocopherols not provided.

Hydrolyzed Jojoba Esters

Hydrolyzed Jojoba Esters mixed with water (20:80 wt.%) are described as a soft white to off-white viscous liquid. The maximum saponification value is 1 mg KOH/g, no trans isomers were detected, the peroxide value was a maximum of 5 meq/kg, and the wax ester content was a maximum of 0.5 area %. The expected shelf life in an unopened container at or below 35°C is 1 year (Floratech 2005d).

Jojoba Alcohol

The properties of Jojoba Alcohol are as follows: specific gravity (25°C) of 0.8499, refractive index (20°C) of 1.4621, acid value of 0.01, saponification number of 0.75, hydroxy value of 178.4, iodine value of 83.1, and freezing point of 12°C (Reinhardt and Brown 1990).

Mixtures

Floratech (2006) analyzed a mixture of isopropyl jojobate, Jojoba Alcohol, Jojoba Esters, and tocopherol (approximate weight % 35:35:30:0.1). It was described as a clear pale yellow liquid at or above room temperature (24°C). Below room temperature, partial crystallization may appear as cloud-like formations which may settle to the bottom. This can be used as is or warmed to remove cloudiness. The product may slightly darken over time. The product was said to have a shelf life of 1 year. The other values reported are listed in Table 4.

Table 3. Chemical properties of 5 Jojoba Ester products (Floratech 2005a,b,c).

Property	Jojoba Ester 15	Jojoba Ester 20	Jojoba Ester 30	Jojoba Ester 60	Jojoba Ester 70
Appearance	Clear, colorless liquid	Creamy white paste	Soft white paste	Firm white paste	Crystalline jojoba wax particles, hard, white, odorless
Saponification Value	88-96 mg KOH/g	88-96 mg KOH/g	88-96 mg KOH/g	88-96 mg KOH/g	88-96 mg KOH/g
Trans isomers	none	none	none	none	none
Acid value	1 mg KOH/g	1 mg KOH/g	1 mg KOH/g	1 mg KOH/g	1 mg KOH/g
Dropping point	10-15°C	42-48°C	47-51°C	56-60°C	-
Iodine value	78-85 g/100 g	64-70g/100 g	57-61 g/100 g	40-44 g/100 g	2 g/100 g
Monounsaturated Esters	-	25-35 area %	40-47 area %	46-53 area %	-
Peroxide value	4 meq/kg	4 meq/kg	4 meq/kg	4 meq/kg	2 meq/kg
Absence of microbial contamination	100 CFU/g	100 CFU/g	100 CFU/g	100 CFU/g	100 CFU/g
Refractive index @ 40°C	1.458-1.460 n_D	-	-	-	-
Specific gravity	0.862-0.867	-	-	-	-
Triglyceride content	1 wt.%	-	-	-	-
Melting Point	-	-	-	-	66-70°C

Table 4. Properties of an Isopropyl Jojobate, Jojoba Alcohol, Jojoba Esters and tocopherol mixture (Floratech 2006).

Property	Value
Dropping point	6 - 12°C
Hydroxyl value	40 - 70 mg/KOH/g
Iodine value	75 - 85 g/100 g
Refractive Index (40°C)	1.452 - 1.454 n_D
Saponification value	80 - 90 mg KOH/g
Specific gravity	0.855 - 0.860
Trans isomers	none detected
Viscosity (25°C)	15 - 25 cP
Acid value	5 mg KOH/g
Peroxide value	3 meq/kg
Absence of microbial contamination	100 CFU/g

Composition

Simmondsia Chinensis (Jojoba) Seed Oil is composed almost completely (97%) of wax esters of monounsaturated, straight-chain acids and alcohols with high-molecular weights (C16-C26). These wax esters exist principally (83%) as combinations of C20 and C22 unsaturated fatty acids and alcohols (McKeown 1983). The long aliphatic chains of both the acids and alcohols make Simmondsia Chinensis (Jojoba) Seed Oil a highly lipophilic chemical (Shani 1983).

The unsaturated fatty acids are mixtures of cis-11-eicosenoic acid (C20) and cis-13-docosenoic acid (C22); small quantities of oleic acid (C18) and cis-15-tetracosenoic acid (C24) are also present. The unsaturated alcohols are mixtures of cis-11-eicosenol, cis-13-docosenol, and cis-15-tetracosenol. Total free acids (C16 to C24) and total alcohols (C16 to C26) each account for 1% of the composition of Simmondsia Chinensis (Jojoba) Seed Oil. Small quantities of sterols (< 0.5%) are also present (McKeown 1983).

Miwa (1971) reported that the composition of Simmondsia Chinensis (Jojoba) Seed Oil was consistent between 2 adjacent regions of Arizona even in samples collected 5 years apart. Simmondsia Chinensis (Jojoba) Seed Oil collected in the California desert had a similar composition to the oil collected in Arizona. However, Simmondsia Chinensis (Jojoba) Seed Oil collected near the ocean in San Diego had a shift in composition toward larger molecule sizes. Simmondsia Chinensis (Jojoba) Seed Oil from an unknown source had shorter chain lengths than the Arizona samples. The major component, eicosenoic acid, was consistent at 35% for all samples.

Simmondsia Chinensis (Jojoba) Seed Oil contains ~0.05% tocopherols (Yaron 1987).

Simmondsia Chinensis (Jojoba) Seed Wax

Yermanos (1975) reported on the Simmondsia Chinensis (Jojoba) Seed Wax from seeds collected weekly for the 8 weeks leading up to maturity. The amount of the wax increased from 13.5% to 49.4% of the seed weight over time. The composition of the wax as characterized by the carbon chain length and the level of saturation also changed over time as shown in Table 5.

Table 5. Fatty acids and alcohols in Simmondsia Chinesis (Jojoba) Seed Wax in immature and mature seeds[A] (Yermanos 1975).

Number of carbon atoms and double bonds	Acids % in seeds collected on:			Alcohols % in seeds collected on:		
	6/20	7/25	8/25	6/20	7/25	8/25
16:0	2.6	0.9	0.8	-	-	-
18:1	16.1	7.7	7.0	-	-	-
20:1	26.3	35.3	36.4	28.4	27.7	28.8
22:0	-	-	-	5.2	5.4	5.4
22:1	5.0	6.0	5.8	16.5	16.9	15.8

[A] Data represent means form 3 bulk wax samples, each from 15 single plant seed samples/date of sampling.

The main constituents of Simmondsia Chinensis (Jojoba) Seed Wax were the wax esters: eicosenyl octadecenoate (C20:1-C18:1; 5.5%), docosenyl eicosenoate (C20:1-C20:1; 21.4%), docosenyl eicosenoate (C22:1-C20:1; 37.8%), eicosenyl docosenoate (C20:1-C22:1), and tetracosenyl eiosenoate (C24:1-C20:1) (Tada et al. 2005).

Jojoba Esters are proper waxes, with no triglyceride components. Jojoba Esters are a complex mixture of long chain (C35 to C46) fatty acids and fatty alcohols joined by an ester bond and do not contain any trans-unsaturation (International Jojoba Export Council 2004).

Floratech (2005a,b) reported the ester chain length and saturation of 4 Jojoba Ester products as shown in Table 6. Each was reported as being 99.95% Jojoba Esters and 0.05% tocopherol.

Table 6. Ester chain length composition and saturation of Jojoba Ester 20, 40, 60, and 80 (Floratech 2005a,b).

Number of carbons and double bonds	% of different chain lenths in Jojoba Ester:			
	20	30	60	70
38:0	1	1	1 - 4	5 - 8
38:1	1 - 2	2 - 4	3 - 4	-
38:2	3 - 5	2 - 4	1 - 3	-
40:0	1 - 2	2 - 4	7 - 18	26 - 34
40:1	8 - 13	14 - 18	18 - 20	-
40:2	20 - 28	17 - 21	5 - 15	-
42:0	1 - 4	2 - 4	6 - 15	44 - 56
42:1	22 - 30	17 - 21	4 - 12	-
42:2	1	2	2 - 5	8 - 12
44:0	2 - 6	4 - 7	4 - 7	-
44:1	2 - 6	4 - 7	4 - 7	-
44:2	5 - 9	4 - 7	1 - 4	-

Floratech (2005b) reported the ester chain length composition of Jojoba Ester 15 as shown in Table 7, without specifying saturation.

Table 7. The ester chain length composition of Jojoba Ester 15 (Floratech 2005b).

Ester chain length	% in Jojoba Ester 15
C 36	2
C 38	5-8
C 40	34-40
C 42	35-44
C 44	11-15
C 46	2

Methods of Manufacture

Jojobutter-51 is an isomorphous mixture of Simmondsia Chinensis (Jojoba) Seed Oil, partially Isomerized Jojoba Oil, and Hydrogenated Jojoba Wax (Brown 1984).

Simmondsia Chinensis (Jojoba) Seed Wax is the product of complete reduction of the unsaturated alcohols and acids comprising the wax ester combinations of Simmondsia Chinensis (Jojoba) Seed Oil (Reinhardt and Brown 1990).

Jojoba Alcohols are prepared via the sodium reduction of Simmondsia Chinensis (Jojoba) Seed Oil and Hydrogenated Simmondsia Chinensis (Joboba) Seed Wax. The alcohols are then further refined to render them suitable for use in cosmetics (Reinhardt and Brown 1990).

Simmondsia Chinensis (Jojoba) Seed Oil is combined with Hydrogenated Jojoba Oil and sodium methylate (catalyst) to get mixed Jojoba Esters (Floratech 2005a). Refined Simmondsia Chinensis (Jojoba) Seed Oil is combined with sodium methoxide to get randomized Jojoba Esters. Tocopherol is then added to make the commercial Jojoba Ester 15 (Floratech 2005b).

Simmondsia Chinensis (Jojoba) Seed Oil is combined with nickel (catalyst) to get Hydrogenated Jojoba Oil. This is converted to powder to get Jojoba Esters (Floratech 2005c). Simmondsia Chinensis (Jojoba) Seed Oil is combined with isopropyl alcohol and sodium methoxide (catalyst) to get isopropyl esters, Jojoba Alcohols, and Jojoba Esters (interesterified [randomized] Simmondsia Chinensis (Jojoba) Seed Oil) in approximately equal amounts (Floratech 2006).

Synthetic Jojoba Oil

Kalscheuer et al. (2006) developed a recombinant strain of *Escherichia coli* that produced an oil that was similar to Simmondsia Chinensis (Jojoba) Seed Oil. Cultivation in the presence of oleate produced $C_{23:1}$, $C_{34:1}$, and $C_{36:2}$ wax esters which were chemically similar to jojoba wax esters. The amounts produced were small.

Analytical Methods

Simmondsia Chinensis (Jojoba) Seed Oil has been analyzed via the following methods: thin layer chromatography (TLC), gas chromatography (GC), nuclear magnetic resonance spectroscopy, infrared spectroscopy, differential scanning calorimetry, and equivalent carbon number analyses (Miwa 1973; Hamm 1984).

Garver et al. (1992) used reversed-phase C_{18} high-performance liquid chromatography (HPLC) coupled with efficient and sensitive detection by an on-line flow-through radiochemical detector to analyze the components of crude jojoba seed homogenate.

Van Boven et al. (1997) used GC, mass spectrometry (MS), gas chromatography/mass spectrometry (GC/MS), and TLC to isolate and identify the phytosterols and fatty alcohols in Simmondsia Chinensis (Jojoba) Seed Oil. Tada et al. (2005) used liquid chromotography/mass spectrometry (LC/MS) and GC/MS analysis to find the main constituents of Simmondsia Chinensis (Jojoba) Seed Wax.

Impurities

The Cosmetic, Toiletry, and Fragrance Association (CTFA) specification for Simmondsia Chinensis (Jojoba) Seed Oil defines positive identification of the oil as a close match to the infrared (IR) spectrum, with no indication of foreign materials (CTFA 1989).

The specification for crude Simmondsia Chinensis (Jojoba) Seed Oil includes less than 0.8 ppm elemental lead (Pb) and less than 0.1 ppm arsenic (as As_2O_3) (Taguchi and Kunimoto 1977).

When Simmondsia Chinensis (Jojoba) Seed Oil was refined via a standard alkali refining process (Swern 1982), a trace amount of nitrogen-containing compounds (6.0 ± 2 ppm) was found (Hamm 1984). Data on the presence and nature of terpenoid compounds were not available.

Jojoba Alcohols contain less than 20 ppm lead and less than 2 ppm arsenic (Reinhardt and Brown 1990).

SGS Canada Inc. (2005a, 2006) analyzed samples of two materials: (1) a mixture of isopropyl jojobate, Jojoba Alcohol and Jojoba Esters, and (2) Hydrolyzed Jojoba Esters and water to determine the presence of impurities (data given in Table 8).

Table 8. Impurities found in a mixture of isopropyl jojobate, Jojoba Alcohol and Jojoba Esters and Hydrolyzed Jojoba Esters and water (SGS Canada Inc. 2005a, 2006).

Impurity	Jojoba mixture	Hydrolyzed Jojoba Esters and water	Detection Limit
As	0.1 µg/g	none	0.1 µg/g
Ca	18 µg/g	none	0.2 µg/g
Cd	none	none	2 methods: 0.1 and 0.2 µg/g
Co	none	none	0.3 µg/g
Cr	none	none	1 µg/g
Cu	6 µg/g	none	0.2 µg/g
Fe	none	1.6 µg/g	2 µg/g
Hg	none	none	0.1 µg/g
K	1 µg/g	10376 µg/g	-
Mg	none	2.5 µg/g	3 µg/g
Mn	none	none	0.7 µg/g
Na	none	72.1 µg/g	10 µg/g
Ni	none	none	2 µg/g
P	none	4.3 µg/g	5 µg/g
Pb	0.8 µg/g	none	0.2 µg/g
Sr	none	none	0.2 µg/g
Zn	4 µg/g	none	0.2 µg/g

SGS Canada Inc. (2005b,c,d,e,f 2006) reported the analysis of Jojoba Esters 15, 20, 30, 60, and 70 as shown in Table 9. Detection limits are not given in Table 9, but were comparable to those shown in Table 8.

USE

Cosmetic

According to information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Ingredient Registration Program (VCRP), Simmondsia Chinensis (Jojoba) Seed Oil was used in a total of 188 cosmetic products, at the time of the original safety assessment, at use concentrations up to 25% (Elder 1989). Currently VCRP data indicated that Simmondsia Chinensis (Jojoba) Seed Oil is used in 1123 products (FDA 2007). A survey of current use concentrations conducted by the CTFA reported use concentrations up to 100% (CTFA 2007). These data are given in Table 10, as a function of product category, along with the total number of products reported in each category. From Table 10, for example, it can be seen that the Seed Oil is used in 109 of a total of 715 conditioners, at a wide concentration range from 0.001 to 67%. In some cases, there were no reported uses to the VCRP, but a current use concentration is provided — for example, the Seed Oil in hair coloring rinses. It should be presumed that there is at least 1 use. In other cases, there is a reported use (Seed Oil in shampoos), but no use concentration is provided.

Simmondsia Chinensis (Jojoba) Seed Wax had no uses listed in 1989 and is currently reported to be used in 8 cosmetic products (FDA 2007) at up to 2% (CTFA 2007).

Hydrogenated Jojoba Oil is reported to be used in 71 cosmetic products, Jojoba Esters in 121 cosmetic products, Hydrolyzed Jojoba Esters in 86 cosmetic products, Simmondsia Chinensis (Jojoba) Butter in 18 cosmetic products, Jojoba Alcohol in 21 cosmetic products, and Synthetic Jojoba Oil in 6 cosmetic products (FDA 2007) at up to 31%, 44%, 2%, 6%, 1%, and 0.1%, respectively (Table 10) (CTFA 2007).

Isomerized Jojoba Oil is not reported as being used, nor were any use concentrations provided.

Apropos of the use of certain of these ingredients in product categories known to be aerosols or sprays, Jensen and O'Brien (1993) reviewed the potential adverse effects of inhaled aerosols, which depend on the specific chemical species, the concentration, the duration of the exposure, and the site of deposition within the respiratory system.

The aerosol properties associated with the location of deposition in the respiratory system are particle size and density. The parameter most closely associated with this regional deposition is the aerodynamic diameter, $\mathbf{d_a}$, defined as the diameter of a sphere of unit density possessing the same terminal setting velocity as the particle in question. These authors reported a mean aerodynamic diameter of 4.25 ± 1.5 μm for respirable particles that could result in lung exposure (Jensen and O'Brien, 1993).

Bower (1999), reported diameters of anhydrous hair spray particles of 60 - 80 μm and pump hair sprays with particle diameters of ≥80 μm. Johnsen (2004) reported that the mean particle diameter is around 38 μm in a typical aerosol spray. In practice, he stated that aerosols should have at least 99% of particle diameters in the 10 - 110 μm range.

Table 9. Impurities found in Jojoba Ester 15, 20, 30, 60, and 70 (SGS Canada Inc. 2005b,c,d,e,f, 2006).[a]

Impurity	Jojoba Esters 15	Jojoba Esters 20	Jojoba Esters 30	Jojoba Esters 60	Jojoba Esters 70
As	none	none	none	none	none
Ca	9 µg/g	none	none	none	none
Cd	none	none	none	none	none
Co	none	none	none	none	none
Cr	none	1 µg/g	1 µg/g	1 µg/g	none
Cu	2 µg/g	none	none	none	none
Fe	none	none	none	5 µg/g	none
Hg	none	none	none	none	none
K	2 µg/g	13 µg/g	2 µg/g	none	3 µg/g
Mg	none	none	none	none	4 µg/g
Mn	0.8 µg/g	none	9 µg/g	none	0.8 µg/g
Na	none	none	none	none	none
Ni	none	none	none	none	2 µg/g
P	none	none	none	none	none
Pb	0.4 ppm	none	0.2 ppm	none	0.5 ppm
Sr	none	none	none	none	none
Zn	none	none	1 µg/g	none	none

[a] Detection limits comparable to those given in Table 8.

Table 10. Historical and current cosmetic product uses and concentrations for Simmondsia Chinensis (Jojoba) Seed Oil, Simmondsia Chinensis (Jojoba) Seed Wax, Hydrogenated Jojoba Oil, Jojoba Esters, Hydrolyzed Jojoba Esters, Simmondsia Chinensis (Jojoba) Butter, Jojoba Alcohol, and Synthetic Jojoba Oil.

Product Category (Total number of products in each category) (FDA 2008)	2007 uses (FDA 2007)	2007 % concentration (CTFA 2007)
Simmondsia Chinensis (Jojoba) Seed Oil		
Baby products		
Lotions, oils, powders, and creams (67)	7	1
Other (64)	2	-
Bath products		
Oils, tablets, and salts (207)	17	0.002-100
Soaps and detergents (594)	15	0.1-5
Bubble baths (256)	3	0.002-2
Capsules (5)	-	2
Other (276)	8	0.08-2
Eye makeup		
Eyebrow pencils (124)	3	0.08-0.1
Eyeliners (639)	20	0.1-4
Eye shadow (1061)	7	0.7-7
Eye lotions (32)	11	0.1-0.5
Eye makeup remover (114)	2	0.1-5
Mascara (308)	2	0.1-1
Other (229)	9	0.1
Fragrance products		
Colognes and toilet waters (948)	-	5
Perfumes (326)	1	5
Powders (324)	1	5
Sachets (28)	-	5
Other (187)	9	5
Noncoloring hair care products		
Conditioners (715)	109	0.001-67
Sprays/aerosol fixatives (294)	12	0.001-1
Straighteners (61)	9	0.01-20
Permanent waves (169)	1	0.01-0.9
Rinses (46)	2	0.01
Shampoos (1022)	51	0.001-2
Tonics, dressings, etc. (623)	30	0.01-4
Wave sets (59)	-	1-2
Other (464)	30	0.1-2[a]
Hair coloring products		
Dyes and colors (1600)	84	0.2
Rinses (15)	-	0.2
Shampoos (1022)	1	-
Color sprays (4)	-	0.3
Bleaches (103)	2	0.05

Table 10 (continued). Historical and current cosmetic product uses and concentrations for Simmondsia Chinensis (Jojoba) Seed Oil, Simmondsia Chinensis (Jojoba) Seed Wax, Hydrogenated Jojoba Oil, Jojoba Esters, Hydrolyzed Jojoba Esters, Simmondsia Chinensis (Jojoba) Butter, Jojoba Alcohol, and Synthetic Jojoba Oil.

Product Category (Total number of products in each category) (FDA 2008)	2007 uses (FDA 2007)	2007 % concentration (CTFA 2007)
Simmondsia Chinensis (Jojoba) Seed Oil (continued)		
Makeup		
Blushers (459)	12	0.4-53
Face powders (447)	10	0.1-53
Foundations (530)	29	0.5-53
Leg and body paints (10)	1	0.1
Lipsticks (1681)	110	1-46
Makeup bases (273)	2	5-53
Rouges (115)	-	12
Makeup fixatives (37)	1	53
Other (304)	24	5-53[b]
Nail care products		
Basecoats and undercoats (43)	2	0.0001-0.2
Cuticle softeners (20)	4	0.1-10
Creams and lotions (13)	-	0.1-25
Extenders (1)	-	0.2
Nail polishes and enamels (398)	20	0.000005-0.001
Nail polish and enamel removers (39)	-	0.0001-0.2
Other (58)	5	0.0001-13[c]
Personal hygiene products		
Underarm deodorants (281)	-	0.002-5
Douches (8)	-	5
Feminine deodorants (7)	-	5
Other (390)	4	0.05-9[d]
Shaving products		
Aftershave lotions (260)	3	0.002-3
Preshave lotions (20)	2	1
Shaving cream (135)	3	0.002-2
Shaving soap (2)	-	0.01
Other (64)	4	0.002
Skin care products		
Skin cleansing creams, lotions, liquids, and pads (1009)	29	0.001-53
Depilatories (49)	3	0.001-53
Face and neck creams, lotions, powder and sprays (546)	67	0.5-53[e]
Body and hand creams, lotions, powder and sprays (992)	106	0.00003-100[f]
Foot powders and sprays (43)	-	53
Moisturizers (1200)	114	0.5-100[g]
Night creams, lotions, powder and sprays (229)	33	0.8-53[h]
Paste masks/mud packs (312)	7	0.5-53
Skin fresheners (212)	3	53
Other (915)	51	1-53[i]

Table 10 (continued). Historical and current cosmetic product uses and concentrations for Simmondsia Chinensis (Jojoba) Seed Oil, Simmondsia Chinensis (Jojoba) Seed Wax, Hydrogenated Jojoba Oil, Jojoba Esters, Hydrolyzed Jojoba Esters, Simmondsia Chinensis (Jojoba) Butter, Jojoba Alcohol, and Synthetic Jojoba Oil.

Product Category (Total number of products in each category) (FDA 2008)	2007 uses (FDA 2007)	2007 % concentration (CTFA 2007)
Simmondsia Chinensis (Jojoba) Seed Oil (continued)		
Suntan products		
Suntan gels, creams, liquids and sprays (138)	3	0.1
Indoor tanning preparations (74)	20	0.0003-2
Other (41)	3	0.1
Total uses/ranges for Simmondsia Chinensis (Jojoba) Seed Oil	**1123**	**0.000005-100**
Simmondsia Chinensis (Jojoba) Seed Wax[j]		
Bath products		
Soaps and detergents (594)	1	0.1
Eye makeup		
Mascara (308)	1	-
Noncoloring hair care products		
Conditioners (715)	-	0.05
Shampoos (1022)	2	0.05
Other (464)	1	-
Shaving products		
Shaving cream (135)	-	2
Skin care products		
Skin cleansing creams, lotions, liquids, and pads (1009)	-	1
Face and neck creams, lotions, powder and sprays (546)	1	-
Body and hand creams, lotions, powder and sprays (992)	1	-
Paste masks/mud packs (312)	1	-
Total uses/ranges for Simmondsia Chinensis (Jojoba) Seed Wax	**8**	**0.05-2**
Hydrogenated Jojoba Oil[k]		
Bath products		
Soaps and detergents (594)	5	0.01-0.5
Other (276)	1	0.1-2
Eye makeup		
Eyeliners (639)	1	-
Eye shadow (1061)	1	2
Eye lotions (32)	1	1
Mascara (308)	30	7
Noncoloring hair care products		
Conditioners (715)	1	-
Sprays/aerosol fixatives (294)	-	0.001
Tonics, dressings, etc. (623)	1	-

Table 10 (continued). Historical and current cosmetic product uses and concentrations for Simmondsia Chinensis (Jojoba) Seed Oil, Simmondsia Chinensis (Jojoba) Seed Wax, Hydrogenated Jojoba Oil, Jojoba Esters, Hydrolyzed Jojoba Esters, Simmondsia Chinensis (Jojoba) Butter, Jojoba Alcohol, and Synthetic Jojoba Oil.

Product Category (Total number of products in each category) (FDA 2008)	2007 uses (FDA 2007)	2007 % concentration (CTFA 2007)
Hydrogenated Jojoba Oil (continued)		
Hair coloring products		
Dyes and colors (1600)		
Hair tints (56)	-	0.1
Rinses (15)	-	0.1
Color sprays (4)	-	0.1
Lighteners with color (14)	-	0.1
Bleaches (103)	-	0.1
Other (73)	-	0.1
Makeup		
Blushers (459)	3	0.1-2
Face powders (447)	-	0.1
Foundations (530)	3	0.1-10
Lipsticks (1681)	1	31
Makeup bases (273)	-	0.1
Makeup fixatives (37)	-	0.1
Other (304)	-	0.1-2
Nail care products		
Creams and lotions (13)	-	0.8
Oral hygiene products		
Other (10)	3	-
Personal hygiene products		
Underarm deodorants (281)	-	0.01
Douches (8)	-	
Feminine hygiene deodorants (7)	-	0.01
Other (390)	-	0.01
Shaving products		
Shaving soap (2)	1	-
Skin care products		
Skin cleansing creams, lotions, liquids, and pads (1009)	9	1-5
Depilatories (49)	-	0.1
Face and neck creams, lotions, powder and sprays (546)	2	0.1[l]
Body and hand creams, lotions, powder and sprays (992)	1	0.01-8[m]
Foot powders and sprays (43)	-	0.1
Moisturizers (1200)	-	0.1[n]
Night creams, lotions, powder and sprays (229)	-	0.1[o]
Paste masks/mud packs (312)	-	0.01-0.4
Skin fresheners (212)	-	0.1

Table 10 (continued). Historical and current cosmetic product uses and concentrations for Simmondsia Chinensis (Jojoba) Seed Oil, Simmondsia Chinensis (Jojoba) Seed Wax, Hydrogenated Jojoba Oil, Jojoba Esters, Hydrolyzed Jojoba Esters, Simmondsia Chinensis (Jojoba) Butter, Jojoba Alcohol, and Synthetic Jojoba Oil.

Product Category (Total number of products in each category) (FDA 2008)	2007 uses (FDA 2007)	2007 % concentration (CTFA 2007)
Hydrogenated Jojoba Oil (continued)		
Suntan products		
Other (41)	1	-
Other (915)	6	0.1
Total uses/ranges for Hydrogenated Jojoba Oil	**71**	**0.001-31**
Jojoba Esters		
Bath products		
Soaps and detergents (594)	7	0.2-2
Other (276)	1	-
Eye makeup		
Eyebrow pencils (124)	1	5
Eyeliners (639)	3	5-14
Eye shadow (1061)	3	0.5-5
Eye lotions (32)	4	0.5-5
Eye makeup remover (114)	-	5
Mascara (308)	6	3-5
Other (229)	2	5
Fragrance products		
Colognes and toilet waters (948)	-	0.05
Perfumes (326)	-	0.002
Other (187)	1	0.8
Makeup		
Blushers (459)	1	7
Face powders (447)	1	3-7
Foundations (530)	14	1-7
Leg and body paints (10)	-	5
Lipsticks (1681)	8	5-44
Makeup bases (273)	2	7
Rouges (115)	-	5-7
Makeup fixatives (37)	1	7
Other (304)	2	5-11[b]
Nail care products		
Basecoats and undercoats (43)	-	18
Cuticle softeners (20)	-	18
Creams and lotions (13)	-	18
Extenders (1)	-	18
Nail polishes and enamels (398)	-	0.5-18
Nail polish and enamel removers (39)	-	18
Other (58)	-	18
Personal hygiene products		
Other (390)	1	2-4[q]

Table 10 (continued). Historical and current cosmetic product uses and concentrations for Simmondsia Chinensis (Jojoba) Seed Oil, Simmondsia Chinensis (Jojoba) Seed Wax, Hydrogenated Jojoba Oil, Jojoba Esters, Hydrolyzed Jojoba Esters, Simmondsia Chinensis (Jojoba) Butter, Jojoba Alcohol, and Synthetic Jojoba Oil.

Product Category (Total number of products in each category) (FDA 2008)	2007 uses (FDA 2007)	2007 % concentration (CTFA 2007)
Jojoba Esters (continued)		
Shaving products		
Aftershave lotions (260)	1	0.002
Other (64)	-	0.000005
Skin care products		
Skin cleansing creams, lotions, liquids, and pads (1009)	26	0.3-10
Depilatories (49)	-	7
Face and neck creams, lotions, powder and sprays (546)	9	0.2-7[r]
Body and hand creams, lotions, powder and sprays (992)	7	0.3-7[r]
Foot powders and sprays (43)	-	7
Moisturizers (1200)	14	7[r]
Night creams, lotions, powder and sprays (229)	4	7[r]
Paste masks/mud packs (312)	1	1-7
Skin fresheners (212)	-	7
Other (915)	1	7
Total uses/ranges for Jojoba Esters	**121**	**0.000005-44**
Hydrolyzed Jojoba Esters		
Fragrance products		
Colognes and toilet waters (948)	53	2
Perfumes (326)	23	0.07
Other (187)	-	0.0002
Noncoloring hair coare products		
Tonics, dressings, etc. (623)	1	-
Shaving products		
Aftershave lotions (260)	7	0.07
Other (64)	-	0.0002
Skin care products		
Face and neck creams, lotions, powder and sprays (546)	1	-
Moisturizers (1200)	1	-
Total uses/ranges for Hydrolyzed Jojoba Esters	**86**	**0.0002-2**
Simmondsia Chinensis (Jojoba) Butter		
Bath products		
Soaps and detergents (594)	2	0.8
Eye makeup		
Mascara (308)	1	6
Makeup		
Lipsticks (1681)	1	3

Table 10 (continued). Historical and current cosmetic product uses and concentrations for Simmondsia Chinensis (Jojoba) Seed Oil, Simmondsia Chinensis (Jojoba) Seed Wax, Hydrogenated Jojoba Oil, Jojoba Esters, Hydrolyzed Jojoba Esters, Simmondsia Chinensis (Jojoba) Butter, Jojoba Alcohol, and Synthetic Jojoba Oil.

Product Category (Total number of products in each category) (FDA 2008)	2007 uses (FDA 2007)	2007 % concentration (CTFA 2007)
Simmondsia Chinensis (Jojoba) Butter (continued)		
Noncoloring hair care products		
Conditioners (715)	1	-
Personal hygiene products		
Other (390)	1	-
Skin care products		
Face and neck creams, lotions, powder and sprays (546)	-	
Body and hand creams, lotions, powder and sprays (992)	6	0.1
Moisturizers (1200)	4	-
Night creams, lotions, powder and sprays (229)	1	-
Other (915)	1	-
Total uses/ranges for Simmondsia Chinensis (Jojoba) Butter	**18**	**0.1-6**
Jojoba Alcohol[s]		
Eye makeup		
Eye shadow (1061)	1	1
Eye Lotion (32)	2	-
Noncoloring hair care products		
Conditioners (715)	-	0.5
Sprays/aerosol fixatives (294)	-	0.5
Straighteners (61)	-	0.1
Permanent waves (169)	-	0.1
Rinses (46)	-	0.1
Shampoos (1022)	-	0.1
Tonics, dressings, etc. (623)	-	0.5
Wave sets (59)	-	0.5
Other (464)	-	0.5
Makeup		
Foundations (530)	2	1
Shaving products		
Shaving cream (135)	-	0.1
Shaving soap (2)	-	0.1
Skin care products		
Face and neck creams, lotions, powder and sprays (546)	1	-
Body and hand creams, lotions, powder and sprays (992)	11	-
Moisturizers (1200)	4	-
Total uses/ranges for Jojoba Alcohol	**21**	**0.1-1**

Table 10 (continued). Historical and current cosmetic product uses and concentrations for Simmondsia Chinensis (Jojoba) Seed Oil, Simmondsia Chinensis (Jojoba) Seed Wax, Hydrogenated Jojoba Oil, Jojoba Esters, Hydrolyzed Jojoba Esters, Simmondsia Chinensis (Jojoba) Butter, Jojoba Alcohol, and Synthetic Jojoba Oil.

Product Category (Total number of products in each category) (FDA 2008)	2007 uses (FDA 2007)	2007 % concentration (CTFA 2007)
	Synthetic Jojoba Oil	
Eye makeup		
Eyeliners (639)	1	-
Noncoloring hair care products		
Conditioners (715)	5	-
Skin care products		
Depilatories (49)		0.1
Total uses/ranges for *Synthetic Jojoba Oil*	6	0.1

[a] 0.1% in a liquid hair lotion, 2% in a hair mask; [b] 5% in a concealer; [c] 0.0001% in a solution used to dilute nail enamel, 10% in a hand and foot exfoliator; [d] 0.05%, 1%, and 9% in body scrubs; [e] 53% in face and neck sprays; [f] 0.00003 - 53 in body and hand sprays; [g] 53% in moisturizing sprays; [h] 5% in night sprays; [i] 1% in an oil stick; [j] listed as Jojoba Wax by the FDA; [k] listed as both Hydrogenated Jojoba Oil and Wax; [l] 0.1% in face and neck sprays; [m] 0.1% in body and hand sprays; [n] 0.1% in moisturizing sprays; [o] 0.1% in night sprays; [p] 2% in a shower gel; [q] 7% in face and neck creams, body and hand sprays, moisturizing sprays, and night sprays; [r] listed as both Jojoba Alcohol and Jojoba (Simondsia Chinensis)

Non-cosmetic

Yaron (1987) reported that jojoba seeds are used by Native American Indians as food and medicine. It is reported that jojoba seeds are good for the stomach, facilitate parturition when mixed with chocolate, and treat sores that erupt on the face. The seeds are also reported to treat sores, scratches, and cuts rapidly; treat suppression of the urine; promote hair growth; and considered a remedy for cancer.

Dweck (1997) reported that the jojoba plant has been used by Native Americans for wound healing and as a skin salve. The expressed juices of the seeds are used to treat eye soreness.

Simmondsia Chinensis (Jojoba) Seed Oil

Non-cosmetic uses of Simmondsia Chinensis (Jojoba) Seed Oil include: high-temperature lubricant for high-speed machinery, sulfurization for extreme-pressure lubricants, treatment of leather, benzene or gasoline-soluble factice for rubber, varnishes, linoleum, or chewing gum, and hydrogenation into hard wax for use as polishing wax, in carbon paper, or as candles that give a brilliant flame with no smoke (Miwa 1973). Jojoba Oil is also used in the pharmaceutical industry as an antifoaming agent in the fermentation of tetracycline and penicillin (Buckley 1981) and as a substitute for sperm whale oil (Scott and Scott 1982).

Simmondsia Chinensis (Jojoba) Seed Oil may be used in the microencapsulation of live cells and enzymes as a drug delivery system (Esquisabel et al. 1997).

Simmondsia Chinensis (Jojoba) Seed Oil is used in pesticides to control white flies. Jojoba products are used for controlling powdery mildew on grapes and on ornamental plants at a concentration ≤1% (Environmental Protection Agency [EPA] 2006).

Simmondsia Chinensis (Jojoba) Seed Wax is used to extract metal ions from aqueous solutions so that the ions may be reused (Binman et al. 1998).

GENERAL BIOLOGY

Absorption, Distribution, Metabolism and Excretion

Simmondsia Chinensis (Jojoba) Seed Oil was detected in the feces of dd Y-S mice (5 weeks old) 1 week after the mice were force-fed doses of 0.5, 0.75, 1.13, and 1.69 mg/10 g. Four groups of 20 mice were evaluated (Taguchi and Kunimoto 1977).

Yaron (1987) reported that nude mouse skin was used to study Simmondsia Chinensis (Jojoba) Seed Oil penetration. After 22 h, there was 6.7-fold more penetration than at 1 h. The cell solution contained ~4 meq Simmondsia Chinensis (Jojoba) Seed Oil/area tested. Based on histological examination of the skin, the main route of penetration was the hair follicle.

Verschuren and Nugteren (1989) tested the effects of Simmondsia Chinensis (Jojoba) Seed Oil on intestinal transit time in 7-week-old, male SPR Wistar rats (Cpb/WU). After 1 week of acclimation on a commercial diet, the diet of the control group (n = 19) was changed to the commercial diet mixed with lard/sunflower seed oil (4:1) with a fat content of 18% (equivalent to 40% energy). The diet of the experimental group was changed to the commercial diet with the lard/sunflower seed oil (9%) and Simmondsia Chinensis (Jojoba) Seed Oil (9%). The rats were fed ad libitum for 10 d, then were trained to eat all of their food in 2 half-hour shifts (7:00 AM to 7:30 AM and 7:00 PM to 7:30 PM). The rats were allowed to eat ad libitum during meal times for 10

d; in the last 3 d, the exact food consumption was recorded. The meals were then adjusted over the next 8 d so that the rats ate exactly the same amount at each meal time.

After a total of 4 weeks, the morning meal was marked by incorporation of [^{3}H]retinol (1 µCi/animal) and the marker carmine (37.5 mg/kg). After 5 h the feces were sampled every 30 min up to 20 h, then hourly up to 33 h, then at 36, 41, 48, 60, 72, 84, and 96 h.

The feces were examined for carmine and the level of radioactivity was determined by liquid scintillation counting. After the subsequent meal, the rats were killed in groups of 4 at 0, 1.5, 3, 6, and 12 hr and the stomach contents sampled, freeze-dried, and weighed.

The treatment group had a lower growth rate (299 ± 4.1 g vs 239 ± 5.3 g). Food consumption over the period of fixed meal times was lower for the Simmondsia Chinensis (Jojoba) Seed Oil-fed rats than for the controls (6.3 ± 0.46 g vs. 5.2 ± 0.78 g). The absolute amounts of radioactivity measured over 96 h were not different between the groups, even with the difference in food consumption. The Simmondsia Chinensis (Jojoba) Seed Oil fed rats excreted more retinol than the control group ($p < .01$), possibly due to reduced retinol absorption. There was no difference in transit time of the radioactivity.

Comparison of the weights of feed consumed and the amount of feed in the rats' stomachs showed that the emptying of the animals' stomachs was not affected by Simmondsia Chinensis (Jojoba) Seed Oil ingestion. No ill effects from the consumption of Simmondsia Chinensis (Jojoba) Seed Oil were reported by the authors.

In a second experiment, the authors fed 10 male rats the treatment diet from the first experiment. After 3 weeks, the rats were anesthetized (2 rats/d) and the ductus thoracicus was cannulated for 1 h. The animals were then killed and the small intestine ligatured and removed. The intestinal mucosa and contents were sampled separately. Lymph was collected. The intestinal mucosa and contents and lymph were analyzed for lipid content as were fecal samples over the previous week by TLC.

The free fatty acids concentration in the intestinal contents was < 5%, with larger amounts in the feces (30%). The authors stated that these findings suggested that hydrolysis of Simmondsia Chinensis (Jojoba) Seed Oil must have continued in the gut beyond the small intestine, possibly by bacteria. Table 11 gives the analysis of the fatty acids and fatty alcohols chain length and saturation found as a function of location (Verschuren and Nugteren 1989).

Simmondsia Chinensis (Jojoba) Seed Wax

Yaron et al. (1980) determined the absorption and distribution of Simmondsia Chinensis (Jojoba) Seed Wax (described as the semisolid fraction of Simmondsia Chinensis (Jojoba) Seed Oil) using 24 male albino mice (5 weeks old; 25-30 g). The animals were divided equally into 4 groups and [^{14}C]Simmondsia Chinensis (Jojoba) Seed Wax (90 ± 10 mg; specific activity 1.14 µCi/g) was injected subcutaneously into the right leg of each animal. Randomly labeled Simmondsia Chinensis (Jojoba) Seed Wax was obtained by exposure of fruiting branches of the shrub (*S. chinensis*) to $^{14}CO_2$ fluxes. The 4 groups of animals were killed 1, 8, 15, and 23 days after injection, and radioactivity in the testis, skin, carcass, and lipid and aqueous fractions of the brain and liver was counted. The results indicated that only a small fraction of the injected [^{14}C]Simmondsia Chinensis (Jojoba) Seed Wax was absorbed. At day 1 post-injection, most of the [^{14}C]Simmondsia Chinensis (Jojoba) Seed Wax was detected in the carcass and in lipid fractions of the brain and liver. In the brain lipid fraction, the amount decreased from 108 ± 46 µg (day 1) to 9 ± 4 µg (day 23), and, in the liver lipid fraction, from 57 ± 16 µg (day 1) to 15 ± 7 µg (day 23). The amount of [^{14}C]Simmondsia Chinensis (Jojoba) Seed Wax in the carcass (100 ± 4 g) was detected on day 1, but not on day 23.

Table 11. Analysis of the fatty acid content (%,) of the semi-synthetic diets containing 9% Simmondsia Chinensis (Jojoba) Seed Oil fed to rats and of the lipids extracted from the various components of the digestive system (Verschuren and Nugteren 1989).

Fatty acid/fatty alcohol chain length/saturation	As given in the diet		As measured in the rat			
	Lard/sunflower seed oil	Jojoba Oil	Lymph	Intestinal mucosa	Intestinal content	Feces
14:0	-	-	0.9	0.7	0.5	0.4
16:0	23.0	-	15.4	14.0	6.0	5.2
16:1 (1)	-	-	2.0	1.5	0.4	0.3
18:0	11.5	-	8.3	12.4	7.0	6.7
18:1 (2)	29.0	10/1[a]	26.3	20.2	15.8	10.2
18:2 (2)	19.0	-	11.2	9.8	5.4	1.5
20:1 (2)	-	71/44[a]	20.6	20.0	39.4	41.9
20:4 (2)	-	-	1.4	3.6	1.9	9.9
22:1 (2)	-	14/45[a]	4.4	4.7	11.9	16.2

[a] Mean of 2 determinations

In a second experiment, 10 albino mice (5 males, 5 females) were injected subcutaneously with [^{14}C]Simmondsia Chinensis (Jojoba) Seed Wax (same dose and specific activity) and killed at intervals after injection. Most of the ^{14}C (>99%) was detected in the carcass. At 8 and 23 days post-injection, the radioactivity TLC profile of carcass lipids indicated that 75% to 83% of the ^{14}C remained in the lipid form in which it had been injected. The remaining ^{14}C was incorporated mainly into neutral lipids, such as triglycerides and fatty acids.

The absorption and distribution of radioactivity from [^{14}C]Simmondsia Chinensis (Jojoba) Seed Wax were further evaluated using 21 male albino mice (5 weeks old; 25-30 g). In this study, the specific activity of [^{14}C]Simmondsia Chinensis (Jojoba) Seed Wax was greater than that used in the preceding 2 experiments. The animals were divided equally into 3 groups, and [^{14}C]Simmondsia Chinensis (Jojoba) Seed Wax was injected subcutaneously into the neck at doses of 9, 23, and 120 mg. Animals were killed 8 days after injection. Following the injection of each dose, radioactivity was detected in the liver, brain, testes, lungs, heart, spleen, kidneys, and carcass lipids, but not in the skin or epididymal fat. The greatest counts of radioactivity were frequently detected in the liver, brain, lungs, and carcass lipids. The smallest amount of radioactivity (all organs included) was detected in the animals injected with 9 mg of [^{14}C]Simmondsia Chinensis (Jojoba) Seed Wax. There were no significant differences between counts of radioactivity in animals injected with 23 mg and those given 120 mg of [^{14}C]Simmondsia Chinensis (Jojoba) Seed Wax (Yaron et al 1980).

Heise et al. (1982) used weanling rats to study the digestibility of Simmondsia Chinensis (Jojoba) Seed Wax. The rats were fed: 1) a standard diet 12% of which was Simmondsia Chinensis (Jojoba) Seed Wax; 2) standard diet with an equivalent amount in calories to the Simmondsia Chinensis (Jojoba) Seed Wax of corn oil; 3) standard diet with an equivalent amount in calories of medium-chain triglycerides; 4) standard diet with equivalent amount in calories of 1:1 mixture of Simmondsia Chinensis (Jojoba) Seed Wax and corn oil; or 5) standard diet with an equivalent amount in calories of 1:1 mixture of Simmondsia Chinensis (Jojoba) Seed Wax and triglycerides. Digestibility was determined during weeks 2 and 4 with the 30-d growth assay.

Weight gain on the Simmondsia Chinensis (Jojoba) Seed Wax diet was half that of the control groups. The mixed diets had minimal weight reduction compared to controls. Digestibility of Simmondsia Chinensis (Jojoba) Seed Wax was 41%. The fecal matter contained 51% fat in the 12% Simmondsia Chinensis (Jojoba) Seed Wax group; this was the only group in which the carcass fat was not increased above baseline level. The efficiency of energy conversion into tissue was half that of the mixed groups and one-third that of the control diets. Biological nitrogen was decreased; the authors suggest that there was an increased use of dietary protein as energy (Heise et al. 1982).

Yaron et al. (1982b) orally administered ^{14}C-Simmondsia Chinensis (Jojoba) Seed Wax (25% in peanut oil;10.9 µCi/g; 0.1 ml) to male albino mice (5 weeks old; n = 20). After 24 h, 10 of the mice were killed and the absoption and distribution of the radioactivity analyzed. The liver and epididymal fat were analyzed in detail using TLC. The remaining 10 mice were killed and analyzed on day 8 after treatment. The experiment was then repeated. Intestinal absorption and distribution of Simmondsia Chinensis (Jojoba) Seed Wax is shown in Table 12. Radiolabel was distirbuted among phospholipids, etc. in the liver and epididymal fat as given in Table 13.

Table 12. Distribution of ^{14}C in the body of mice 1 and 8 days after oral administration of ^{14}C-labeled Simmondsia Chinensis (Jojoba) Seed Wax (Yaron et al. 1982b).

	^{14}C sp act in the tissue (dpm/g wet tissue ± SE)			
	1st Run		**2nd Run**	
Tissue	**Day 1**	**Day 8**	**Day 1**	**Day 8**
Liver lipids	805 ± 88	136 ± 13	1570 ± 390	776 ± 280
Heart	2140 ± 880	980 ± 78	2080 ± 328	904 ± 248
Lungs	Not determined	Not determined	2300 ± 308	1170 ± 296
Spleen	2020 ± 560	685 ± 82	2300 ± 404	1180 ± 330
es	1266 ± 360	974 ± 196	1180 ± 224	772 ± 150
Kidneys	2964 ± 674	984 ± 32	3720 ± 544	1404 ± 310
Muscle	1414± 290	1346 ± 578	1210 ± 194	882 ± 136
Epididymal fat	3770 ± 430	1740 ± 770	7760 ± 2160	4460 ± 1335

Table 13. Radioactivity TLC profile of liver and epididymal fat lipids one day after ingestion of ^{14}C-labeled Simmondsia Chinensis (Jojoba) Seed Wax (Yaron et al. 1982b).

	Incorporation of ^{14}C into lipid fraction (%)		
R_f	Liver	Epididymal fat	Lipid standards
0.03	27.0 ± 3.1	0	Phospholipids and glycolipids
0.08	5.5 ± 0.5	5.7 ± 3.2	Cholesterol
0.19	5.5 ± 3.2	0	Fatty acids
0.31 - 0.35	51.3 ± 6.8	92.0 ± .02	Triglycerides
0.80	11.6 ± 3.7	4.3 ± 4.1	Wax esters and cholesterol esters

Penetration Enhancement

Simmondsia Chinensis (Jojoba) Seed Oil

Schwarz et al. (1996) tested the effectiveness of Simmondsia Chinensis (Jojoba) Seed Oil, in the form of submicron particles of oil-in-water emulsion, for the delivery of diclofenac diethylammonium. The emulsion consisted of Simmondsia Chinensis (Jojoba) Seed Oil (20%) and diclofenac (diethyl ammonium salt; 1.16%) prepared by a proprietary high pressure homogenization process. Wistar rats (n = 6) were anaesthetized and iota-carrageenan (100 µl; 1%) was injected into the plantar region of a hind paw. The rats were then topically treated with the Jojoba emulsion, a commercial anti-inflammatory cream with the same concentration of diclofenac, or nothing. Edema volume was measured at 0, 0.5, 1, 2, 3, 4, and 6 h. There were no signs of skin irritation observed. Anti-inflammatory activity in the Jojoba emulsion was evident at 1 h. At 3, 4, and 6 h, the edema in the Jojoba emulsion group was less than that of the commercial cream ($p < .05$). The relative activity for the control, commercial cream, and the Jojoba emulsion were 100 ± 16%, 79 ± 14%, and 46 ± 18%. The authors concluded that the jojoba emulsion can be used to deliver moisturizing agents and lipids to the skin in cosmetics.

El laithy and El-Shaboury (2002) found that an emulsion of brij 96 (surfactant), capmul (cosurfactant), and Simmondsia Chinensis (Jojoba) Seed Oil with 40% water delivered fluconazole through new born mouse skin in a Franz diffusion cell at a greater rate than gel bases (cetyl palmitate; mixture of glyceryl stearate, cetearyl alcohol cetyl palmitate, and cocoglycerides; glyceryl stearate; and glyceryl monostearate) at 10% and 30%.

Wang et al. (2007) tested the dermal penetration enhancement properties of essential oils and plant oils including Simmondsia Chinensis (Jojoba) Seed Oil (10%). The oils were incorporated into microemulsions containing Span and Tween as emulsifying agents and aminophylline (5%). The attenuated total reflection was measured on the forearms (7 x 2 cm) of subjects (n = 6) before application and 30 and 60 min after application of the emulsion (~ 0.3 g). Simmondsia Chinensis (Jojoba) Seed Oil increased the permeability of the stratum corneum to aminophylline in comparison with treatment with aminophylline alone. The hierarchy of penetration enhancement of the plant and essential oils was: Simmondsia Chinensis (Jojoba) Seed Oil > peppermint > lilacin = rosemary = corn germ > ylang > olive. The authors concluded that the choice of proper combination of oil phase lipids may allow drug-controlled delivery from a topical oil/water microemulsion.

Shevachman et al. (2008) tested the enhancement of diclofenac sodium by microemulsions of Simmondsia Chinensis (Jojoba) Seed Oil/hexanol/Brij 96V/water and compared it with similar micoemulsions containing paraffin oil and isopropyl myristate. For comparison, an emulsion with Voltaren Emulgel (a commercial cream containing 1.16% diclofenac diethylammonium, corresponding to 1% diclofenac sodium) was used. The emulsions containing diclofenac sodium (0.5 ml) were applied to the trimmed abdominal area of anesthetized Sprague-Dawley rats in open containers glued to the skin. Blood samples were taken at 1, 2, 4, 6, and 8 h and analyzed for diclofenac. There was similar penetration of diclofenec with the Simmondsia Chinensis (Jojoba) Seed Oil emulsion as the commercial cream (C_{max} = 0.116 ± 0.031 and 0.106 ± 0.006 mg/ml and area under the curve = 0.601 ± 0.107 and 0.558 ± 0.172 µg/ml/h, respectively). The paraffin oil and isopropyl myristate emulsions had great penetrations (C_{max} = 0.962 ± 0.191 and 0.845 ± 0.005 mg/ml and area under the curve = 4.545 ± 0.615 and 4.067 ±0.482 µg/ml/h, respectively).

In an in vitro study, the abdominal skin of freshly killed rats was clipped, washed, and the subcutaneous fat removed. The skin was installed onto Franz diffusion cells with the stratum corneum facing upwards. Microemulsions or Voltaren Emulgel (0.5 g) were applied to the skin. Samples of the receptor cell were taken periodically. The microemulsions consisted of Simmondsia Chinensis (Jojoba) Seed Oil/hexanol at 1:1 wt ratio (60%) and Brij 96 or Tween 60 (40%) with diclofenac sodium (1%) added.

The Simmondsia Chinensis (Jojoba) Seed Oil emulsion had lower penetration of diclofenac than did paraffin oil or isopropyl myristate, which were similar. The drug permeability in the Simmondsia Chinenesis (Jojoba) Seed Oil was higher than the commercial cream, unlike the in vivo test. The authors suggest

that this could be due to the optimal perfusion and hydration of the skin in the diffusion cells compared to the skin in the animal study. The authors concluded that Simmondsia Chinensis (Jojoba) Seed Oil did not increase penetration of dicofenac through the skin and seemed to prevent active molecules from being freely diffused into the skin. The authors suggest that the 3-dimensional structure of the oil may result in delaying the diffusion of the drug (Shevachman et al. 2008).

Anti-inflammatory Effects

Jojoba Liquid Wax Habashy et al. (2005) investigated the anti-inflammatory effects of what the authors referred to as jojoba liquid wax in several experiments. In the first experiment, adult male Sprague-Dawley rats were used. The rats were fasted with free access to water for 16 h before treatment. Five groups (n = 6) of rats were treated. Groups I and II were administered saline by intubation; Groups III and IV were administered jojoba liquid wax (5 ml/kg (~4.35g) or 10 ml/kg (~8.7 g), respectively); and Group V was administered indomethacin (a standard anti-inflammatory drug; 10 ml/kg). Thirty min later, Group I was administered saline (0.05 ml) and Groups II through V were administered carrageenin (0.05 ml; 1% in saline) subcutaneously on the plantar surface of the right hind paw. The volume of the paw was immediately measured by water displacement and again 3 h later.

The right hind paws were removed after killing the rats. The eicosanoid-containing fluid was removed with the use of 10 μM indomethacin in 0.1 ml saline.

The carrageenin injection resulted in severe inflammation and increase in mean volume of the paw (162.3%) compared to untreated paws. Pretreatment with jojoba liquid wax at both doses (5 or 10 ml/kg) inhibited the carrageenin-induced increase in edema volume by 26.4% and 34%, respectively. Indomethacin treatment reduced inflammation by 43.4%.

Carrageenin injection resulted in a 5-fold increase in prostaglandin E_2 (PGE_2) concentration in Group II compared to the untreated Group I. Jojoba liquid wax reduced the PGE_2 concentration by 58.15% and 77.4%, respectively. The 10 ml/kg dose of jojoba liquid wax and the indomethacin lowered the PGE_2 to almost normal levels.

The authors conducted a chick's embryo chorioallantoic membrane (CAM) test. Fertile chicken eggs were incubated for 8 d then divided into 4 groups (n = 6). Filter paper discs (10 mm in diameter) were placed on the surface of the CAM after opening the shells with a dental drill. The shell pieces were replaced and sealed with paraffin wax. The filter paper in Group I was not treated (control); Groups II and III were treated with jojoba liquid wax (3.5 (~3.05 mg; 30%) and 7 μl (~6.1 mg; 50%), respectively) in saline. Group IV was treated with indomethacin (2.5 μg). The eggs were incubated for 4 d and opened by cutting the shells circumferentially along the longer perimeter. CAM membranes were eased out of the shell and the disc (with any adhering or infiltrating granulation tissue) were cut with fine scissors. The discs and tissue were dried overnight and weighed individually.

The administration of jojoba liquid wax at 30% and 50% decreased the granulation tissue weight by 15.8% and 38%, respectively, compared to the control.

The authors induced ear edema in rats to assess the effects of jojoba liquid wax. Five groups of rats (n = 6) were treated topically: Group I was treated with solvent; Group II was treated with irritant (4 parts croton oil, 10 parts ethanol, 20 parts pyridine, 66 parts ethyl ether) and solvent; Groups III and IV were treated with irritant, jojoba liquid wax (30% or 50%, respectively), and solvent; and Group V was treated with irritant, solvent, and indomethacin (12.5% w/v). Each solution was administered in a volume of 20 μl on both sides of the right ear. The left ear was left untreated and served as the control. One h after treatment, the right ears were treated again (Group I, solvent; Groups II through V croton oil solution). After 4 h, the rats were killed. An 8-mm cork borer was used to punch a disc out of each ear; the discs were weighed immediately.

The entire ear was homogenized in buffer and centrifuged and used to calculate myeloperoxidase (MPO) activity. Protein content was determined. Representative ear tissue was fixed, embedded, and sectioned for microscopic examination regarding leukocytic infiltration, edema, and extravasations.

Application of croton oil caused the ear disc to increase in size by 216% over the control. Pretreatment with jojoba liquid wax (30% and 50%) reduced the increase by 28% and 43.6%, respectively. MPO activity in ears treated with croton oil increased 83-fold. Pretreatment with jojoba liquid wax decreased MPO activity by 29% ($p < .05$) and 53.3% ($p < .05$), respectively, compared to ears not treated with jojoba liquid wax. Indomethacin treatment reduced MPO activity ($p < .05$). Ears treated with croton oil and no jojoba liquid wax had massive neutrophil infiltration with extraversion of red blood cells as well as edema in the dermal layer. Ears treated with jojoba liquid wax had less neutrophil infiltration and less hyperemia in a dose dependent manner.

The authors divided 30 rats into 5 groups (n = 6) and injected each of them with 20 ml sterile air in the suprascapular area of the back. Three days later, the pouches were re-inflated with 10 ml sterile air. After another 3 days, lipopolysaccharide from *E. coli* serotype 0111:B4 (LPS; 100 μg/ml) in physiological saline (1 ml/kg) was injected into the air-formed pouches of Groups II through V.

Group I was administered only saline. The rats were treated 30 min later: Groups I and II were administered only saline; Groups III and IV were administered jojoba liquid wax (5 and 10 mg/kg, respectively); and Group V was administered indomethacin (10 mg/kg). Eight h later, the pouches were lavaged using 1 ml sterile physiological saline. The lavage fluid was centrifuged and analyzed for nitric oxide (NO) and tumor necrosis factor-α (TNF-α).

The air pouch caused a 60-fold increase of NO production compared to untreated animals. Jojoba liquid wax injection at 5 and 10 ml/kg reduced NO levels by 31.4% ($p < .05$) and 32.8% ($p < .05$), respectively, compared to Group II. Indomethacin

lowered NO levels by 36.6% ($p < .05$). There was an 8-fold increase in TNF-α levels compared to untreated animals. Jojoba liquid wax treatment at 5 and 10 ml/kg lowered TNF-α levels by 62.2% ($p < .05$) and 75.8% ($p < .05$), respectively. Jojoba liquid wax (at 30% and 50%) reduced MPO activity by 29% and 53.3%, respectively.

The authors concluded that jojoba liquid wax exerted anti-inflammatory activity in several animal models; jojoba liquid wax combats inflammation via multilevel regulation of inflammatory mediators (Habashy et al. 2005).

Blood Cholesterol Effects

The effects of ingested Simmondsia Chinensis (Jojoba) Seed Oil on blood cholesterol concentrations were evaluated using 4 groups of female New Zealand white rabbits (4 months old; n = 4). The following diets (100 g of chow per diet) were provided daily for 30 days: (group 1) chow supplemented with 2% Simmondsia Chinensis (Jojoba) Seed Oil, (group 2) chow containing 1% cholesterol and 2% Simmondsia Chinensis (Jojoba) Seed Oil, (group 3) chow containing 1% cholesterol supplemented with 6% Simmondsia Chinensis (Jojoba) Seed Oil, (group 4) chow supplemented with 1% cholesterol (cholesterol control), and (group 5) untreated chow (negative control). Uneaten chow was discarded each day. The study was repeated using different groups of rabbits. Blood cholesterol concentrations were slightly increased in rabbits fed a cholesterol-free diet containing 2% Simmondsia Chinensis (Jojoba) Seed Oil. Rabbits fed an atherogenic diet consisting of 1% cholesterol and 2% Simmondsia Chinensis (Jojoba) Seed Oil had a 40% decrease in blood cholesterol over that of the cholesterol control. There was no further decrease in blood cholesterol concentrations in rabbits fed a diet containing 1% cholesterol and 6% Simmondsia Chinensis (Jojoba) Seed Oil for an additional 30-day period (Clarke and Yermanos 1981).

Miscellaneous Studies

Simmondsia Chinensis (Jojoba) Seed Oil

Week and Sevigne (1949a) reported that Simmondsia Chinensis (Jojoba) Seed Oil contains factors inhibiting the hydrolysis of vitamin A esters in chicks.

Week and Sevigne (1949b) reported that Simmondsia Chinensis (Jojoba) Seed Oil contains factors inhibiting the hydrolysis of vitamin A esters in rats to a greater extent than corn oil.

Acute Animal Oral Toxicity

Simmondsia Chinensis (Jojoba) Seed Oil

The oral toxicity of crude Simmondsia Chinensis (Jojoba) Seed Oil was evaluated using 80 5-week-old, dd Y-S mice. The average weights of 40 male and 40 female mice were 22.5 and 21.3 g, respectively. The animals were divided equally into 4 groups (10 males, 10 females/group), and Simmondsia Chinensis (Jojoba) Seed Oil was administered via gastric intubation at a single dose of 0.5, 0.75, 1.13, or 1.69 ml/10 g of body weight. Feed was withheld 6 h prior to intubation. At 7 d post-administration, the animals were killed and necropsied. Peritonitis was observed in 1 animal dosed with 1.69 ml/10 g, and discoloration of the renal capsule was observed among all groups. None of the gross alterations observed, including the single death, were attributed to the administration of Simmondsia Chinensis (Jojoba) Seed Oil. The actual causes of these deaths were not reported (Taguchi and Kunimoto 1977).

Following the administration of a single dose of Simmondsia Chinensis (Jojoba) Seed Oil (21.5 ml/kg) to male albino rats (number and weights not stated), fewer than 50% of the animals died (Wisniak 1977).

The acute oral toxicity of a lip balm product containing 20.0% Simmondsia Chinensis (Jojoba) Seed Oil was evaluated using 10 Sprague-Dawley rats (5 males, 5 females; weights not stated). A single oral dose (5.0 g/kg) was administered to each animal via gavage. The animals were fasted during the night prior to dosing. None of the animals died during the 15-day observation period, and the product was classified as nontoxic (CTFA 1985a).

Simmondsia Chinensis (Jojoba) Seed Wax

The acute oral toxicity of a 50.0% solution of Simmondsia Chinensis (Jojoba) Seed Wax in corn oil (dose = 5.0 g/kg) was evaluated according to the procedure described above using 10 albino Sprague-Dawley rats (5 males, 5 females; 200-300 g). The only procedural variation was a 4-day observation period after dosing. Simmondsia Chinensis (Jojoba) Seed Wax was not classified as a toxic substance. Neither the mortality rate nor the results of macroscopic examinations were reported (Reinhardt and Brown 1990).

Jojoba Esters

Leberco Testing, Inc. (1988a) orally administered a single dose of Jojoba Esters 15 (5 g/kg) to white rats (n = 10; 5 male, 5 female) after 18 h of fasting as described in the Federal Hazardous Substances Act (Consumer Product Safety Commission 2007). The rats were observed for signs of toxicity for 14 d then necropsied. All the rats survived. There were no signs of toxicity.

Leberco Testing, Inc. (1988b) orally administered a single dose of Jojoba Esters 30 (5 g/kg) to white rats (n = 10; 5 male, 5 female) after 18 h of fasting. The rats were observed for signs of toxicity for 14 d then necropsied. All rats survived and there were no signs of toxicity.

Leberco Testing, Inc. (1988c) orally administered a single dose of Jojoba Esters 60 (5 g/kg) to white rats (n = 10; 5 male, 5 female) after 18 h of fasting. The rats were observed for signs of toxicity for 14 d then necropsied. All the rats survived. There were no signs of toxicity.

Leberco Testing, Inc. (1988d) orally administered a single dose of Jojoba Esters 70 (5 g/kg; 50% in corn oil) to albino Sprague Dawley rats (n = 10; 5 male, 5 female) after 18 h of fasting. The rats were observed for signs of toxicity for 14 d then necropsied. All the rats survived. There were no signs of toxicity.

In another study, the acute oral toxicity of 2 Jojoba Esters (iodine values 40 and 60) was evaluated using 2 groups of 10 white rats (5 males, 5 females per group). Animal weights ranged from 208 to 238 g in one group and from 212 to 238 g in the other group. Feed was withheld for 18 h, and the test substance (dose = 5.0 g/kg) was administered via a rigid stomach tube. The animals were then observed for signs of toxicity during a period of 14 days; all of the animals survived. At the conclusion of the observation period, the animals were killed and internal organs examined macroscopically. No gross abnormalities were observed in either test group (Reinhardt and Brown 1990).

Jojoba Alcohol

The acute oral toxicity of Jojoba Alcohol was evaluated using 3 groups of 20 mice of the dd Y-S strain (weights not stated). The test substance was administered via stomach tube to the 3 groups at doses of 32, 40, and 50 ml/kg, respectively. None of the animals in any of the 3 groups died (Taguchi no date).

Short-term Oral Toxicity

Simmondsia Chinensis (Jojoba) Seed Oil

The oral toxicity of refined Simmondsia Chinensis (Jojoba) Seed Oil was evaluated using 4 groups of 10 male Sprague-Dawley rats (avg. weight 80.6 g). Two of the groups were fed basal diets (5 g/feeding) containing 0.5 or 1.0 g of Simmondsia Chinensis (Jojoba) Seed Oil once daily for 7 days. The remaining 2 groups were fed basal diets containing 2.0 or 3.0 g of Simmondsia Chinensis (Jojoba) Seed Oil once daily for 4 d. The animals were given water ad libitum. Signs of toxicity were observed in 5 of the rats that were fed 1.0 g of Simmondsia Chinensis (Jojoba) Seed Oil (in diet) and all of the rats fed 2.0 and 3.0 g of Simmondsia Chinensis (Jojoba) Seed Oil. The mortality rate was 10% in each of these 3 groups. None of the rats fed 0.5 g of Jojoba Oil died (Hamm 1984).

Verschuren (1989) fed Simmondsia Chinensis (Jojoba) Seed Oil to male and female SPF Wistar rats (6 weeks old at acclimation) for 4 weeks. The rats were fed a purified diet with Simmondsia Chinensis (Jojoba) Seed Oil at 0 (n = 12), 2.2% (n = 10), 4.5% (n = 10), and 9% (n = 12). After 6 d on the diet, 2 of each sex in the control and high dose groups were killed and the hearts examined for fat deposition. After 3 weeks on the diet, blood was collected and analyzed. After 4 weeks on the diet, the feces were sampled and analyzed for lipid content. At the end of the experiment, the rats were killed and necropsied, blood collected and analyzed, and tissues were histologically examined.

No deaths occurred during the experiment. All the rats appeared to be in good health and no clinical signs were observed. There was a dose-dependent growth retardation in both sexes. Feed intake and water consumption did not differ between the groups. The amount of feces produced increased with Simmondsia Chinensis (Jojoba) Seed Oil intake. The lipid content of the feces had a dose-dependent increase (up to > 6-fold). There were no hematological differences except for the white blood cell count which increased in the high dose group in both males (13.6 ± 0.67 vs 16.9 ± 1.02) and females (13.7 ± 0.90 vs 21.0 ± 2.03). Serum analysis showed an increase enzyme activities (isocitrate dehydrogenase [ICDH], saccharopine dehydrogenase [SDH], alkaline phosphatase [ALP], aspartate aminotransferase [AST], alanine aminotransferase [ALT], hydroxybutyrate dehydrogenase [α-HBDH], and creatine kinase [CK]). Urea concentrations increased in a dose dependent manner. A negative correlation was found for creatine and triacylglycerols and dose levels.

Animals fed Simmondsia Chinensis (Jojoba) Seed Oil had less body fat deposition. Absolute weights of the organs decreased for both sexes except for the spleen in the females. There was no evident adverse effect to the heart after 6 d of the Simmondsia Chinensis (Jojoba) Seed Oil diet. The stomachs of the rats fed Simmondsia Chinensis (Jojoba) Seed Oil were much fuller compared to the controls. The small intestines were distended and the contents were more fluid and non-homogenous compared to controls. The contents of the cecum were coarse and heterogenous compared to controls. The jejunum and ileum of the treatment groups were characterized by massive vacuolization of the enterocytes, distension of the lamina propria, and an increase in cellular components. There was increased cell turnover in the crypts of Lieberkuhn.

In a second experiment, 2 groups of rats (n = 5) were fed the diet with either 0 or 9% Simmondsia Chinensis (Jojoba) Seed Oil . After 3 weeks, the rats were killed and the small intestine removed and examined. The entire small intestine was affected except the anterior section of the duodenum and the posterior section of the ileum. There was an accumulation of fat in the vacuoles of the enterocytes in the upper region of the villi. The ALP activity was decreased. In the livers, there was a slight increase in intracellular acidophilic vacuoles, acidophilic bodies, and the number of mitoses (Verschuren 1989).

Dermal

Jojoba Alcohol

Taguchi (no date) evaluated the dermal toxicity potential of Jojoba Alcohol using 10 white male rabbits. Jojoba Alcohol was tested at concentrations of 12.5, 25.0, and 50.0% (in refined Simmondsia Chinensis (Jojoba) Seed Oil). Oleyl alcohol, also tested at concentrations of 12.5, 25.0, and 50.0% (in refined Simmondsia Chinensis (Jojoba) Seed Oil), served as the control.

In 15- and 30-day tests, there were no reactions to 12.5% Jojoba Alcohol that were grossly visible. However, the results of

microscopic examinations were that reactions ranged from very light to light incrassation of the germinative zone of the epidermis in 4 rabbits (15-day test), and reactions ranging from very light to medium incrassation of the germinative zone and very light to light dermal infiltration in 4 rabbits (30-day test). Also, in the 15-day test, 25.0% Jojoba Alcohol induced redness (2 rabbits), and redness and induration (1 rabbit); 50.0% Jojoba Alcohol induced redness (1 rabbit), redness and induration (2 rabbits), and redness, induration, and swelling (1 rabbit). In the 30-day test, 25.0% Jojoba Alcohol induced redness (2 rabbits); 50.0% Jojoba Alcohol induced redness (2 rabbits) and redness, induration, and swelling (2 rabbits). Histopathological evaluations in both the 15- and 30-day tests were negative for any reactions that were more severe than light incrassation of the germinative zone of the epidermis or very light dermal infiltration (Taguchi no date).

Subcutaneous

Simmondsia Chinensis (Jojoba) Seed Wax

The subcutaneous toxicity of Simmondsia Chinensis (Jojoba) Seed Wax was evaluated using 3 groups of 6-week-old male rats (10 rats/group). The 2 experimental groups received subcutaneous injections of Simmondsia Chinensis (Jojoba) Seed Wax (1 ml/kg of body weight) 6 days per week for 7 weeks. Refined olive oil was administered to the control group according to the same procedure. At the end of the seventh week, 10 experimental animals and 5 controls were killed. The remaining animals were killed 6 weeks later. Urine tests, blood tests, and gross and microscopic examinations were performed. There were no traces of bilirubin, ketones, glucose, or urobilinogen in the urine of any of the tested animals. Occult blood was detected in the urine of 7 experimental animals and 5 controls. Additionally all experimental animals and 5 controls had proteinuria. The urinary protein could have resulted from the contamination of urine with traces of feed. Most of the results from blood chemistry and blood cell analyses were similar in experimental and control groups. Except for a slight increase in liver weight relative to the increase in body weight (experimental animals), there were no significant differences in body weight or organ weight between experimental and control groups. Microscopic changes were not observed in the skin or in any of the other organs examined (Yaron et al 1982b).

Subchronic Dermal Toxicity

Simmondsia Chinensis (Jojoba) Seed Wax

The subchronic dermal toxicity of refined Simmondsia Chinensis (Jojoba) Seed Wax was evaluated using 32 DH guinea pigs (320 ± 25 g). The animals were divided into 4 groups (4 males, 4 females/group). In the first 2 groups, Simmondsia Chinensis (Jojoba) Seed Wax was applied to shaved dorsal skin in doses of 0.25 and 0.5 g/kg, respectively. Applications were made 6 days per week for a total of 20 weeks. The application sites were not covered. The 2 control groups received applications of olive oil (0.5 g/kg) and saline, respectively, according to the same procedure. At the end of the treatment period, the animals were killed and gross and microscopic examinations were performed. There were no differences in body weights or organ weights (liver, heart, kidneys, and testes) between the 4 groups of guinea pigs. Furthermore, lesions were not observed in tissues from the following organs (all groups): adrenal gland, thyroid gland, kidney, urinary bladder, spleen, liver, pancreas, heart, brain (2 sections), stomach, small and large intestine, and skin from treated and untreated areas (Yaron et al. 1982a).

Chronic Toxicity

No chronic toxicity data were available.

Dermal Irritation and Sensitization

Jojoba Alcohol

The primary skin irritation potential of Jojoba Alcohol (10.0% w/w in refined Simmondsia Chinensis (Jojoba) Seed Oil) was evaluated using 10 male and 10 female albino marmots with the Draize test (Taguchi no date). The test substance (0.5 ml) was applied, under a one-inch patch secured with adhesive tape, to each animal. The animals were immobilized in an animal holder, and the entire trunk of each animal was wrapped with rubberized cloth that remained throughout the 24 h exposure period. Reactions were scored at 24 and 48 h post-application according to the scales: 0 (no erythema) to 4 (severe erythema to slight eschar formation); 0 (no edema) to 4 (severe edema). Reactions to the test substance were not observed in any of the animals tested.

The skin sensitization potential of Jojoba Alcohol (10.0% w/w in refined Simmondsia Chinensis (Jojoba) Seed Oil) was evaluated according to the maximization test using 10 male and 10 female albino marmots. Two groups of male and female marmots (10 animals per sex) served as the untreated controls. Initially, each of the following substances (0.05 ml) was injected at different paired sites, to the right and left of the midline, on the back of each animal: complete adjuvant/water (1/1 mixture), Jojoba Alcohol solution, and complete adjuvant/Jojoba Alcohol solution (1/1 mixture). The Jojoba Alcohol solution consisted of Jojoba Alcohol dissolved in refined Simmondsia Chinensis (Jojoba) Seed Oil (1/10 mixture). After 1 week, patches containing the 10.0% Jojoba Alcohol solution (0.5 ml) were applied to the same injection sites. Two weeks later (challenge phase), a patch containing the solution was applied to a new site that was posterior to the injection sites. No sensitization reactions were observed 24 or 48 h after application of the challenge patch.

In an additional study connected with the SHORT-TERM TOXICITY study above, the dermal irritation potential of Jojoba Alcohol (12.5, 25.0, and 50.0%; in refined Simmondsia Chinensis (Jojoba) Seed Oil) using white male rabbits (n = 10) was tested. Each animal was simultaneously patch tested (6 patches per animal) with the 3 concentrations of both the test substance and control; patches were applied to the back. The 2 repeated patch

tests performed involved 15 days of patch testing (5 rabbits) and 30 days of continuous patch testing (5 rabbits), respectively. Naked eye observations of reactions were made, according to the method of Draize, on the last day of each test.

The average skin irritation scores during the 15-day test were as follows: 12.5% Jojoba Alcohol (no reactions), 25.0% Jojoba Alcohol (0.2-0.8), and 50.0% Jojoba Alcohol (0.4-1.80). During the 30-day skin irritation test, the average skin irritation scores were as follows: 12.5% Jojoba Alcohol (0.5), 25.0% Jojoba Alcohol (0.2 to 1.0), and 50.0% Jojoba Alcohol (0.6 to 1.25). The results of skin irritation tests on 12.5, 25.0, and 50.0% Jojoba Alcohol were not considered different from those for the controls, 12.5, 25.0, and 50.0% oleyl alcohol (Taguchi no date).

Simmondsia Chinensis (Jojoba) Seed Oil

The skin irritation potential of refined Simmondsia Chinensis (Jojoba) Seed Oil (100%) was evaluated using 10 male albino guinea pigs (weights = 350 g; strain not stated). Olive oil and light liquid paraffin served as controls. Half of the animals were simultaneously patch tested with Simmondsia Chinensis (Jojoba) Seed Oil (0.5 ml) and each control (0.5 ml) daily for 15 days. Applications were made to shaved skin. The remaining animals were patch tested (same procedure) daily for 30 days. Reactions were scored according to the Draize scale: 0 (no erythema or edema) to 4 (severe erythema to slight eschar formation, and edema). No significant reactions to Simmondsia Chinensis (Jojoba) Seed Oil or olive oil were observed. However, flare reactions to liquid paraffin were observed on the third day of the study. The results of microscopic examinations indicated no edema or cellular infiltration. However, swelling of the epidermis and hypertrophy at the roots of hairs were evident in all groups. Swelling of the epidermis may have been due, in part, to the shaving of application sites (Taguchi and Kunimoto 1977).

The skin irritation potential of a lip balm product containing 20.0% Simmondsia Chinensis (Jojoba) Seed Oil was evaluated using 6 New Zealand white rabbits. A single 24 h application of the test substance (0.5 ml) was made to abraded and intact skin of the back. The test sites were covered with occlusive patches during the 24-h period. At 24 and 72 h post-application, reactions (erythema and edema) were scored according to the Draize scale: 0 to 4. The product was considered minimally irritating (mean primary irritation score = 0.33) (CTFA 1985b).

Simmondsia Chinensis (Jojoba) Seed Wax

The preceding experimental procedure was used to evaluate the skin irritation potential of Simmondsia Chinensis (Jojoba) Seed Wax (100%) in 6 albino rabbits (ages not stated). Positive skin irritation reactions were defined as primary irritation scores of 5 or greater. The mean primary irritation score for Simmondsia Chinensis (Jojoba) Seed Wax was 0.17 (Reinhardt and Brown 1990).

Jojoba Esters

Leberco Testing, Inc. (1988e) applied Jojoba Esters 15 to the intact and abraded skin of albino rabbits (n = 6). The rabbits were clipped of 10% their body hair; half of the exposed skin area was left intact and the other half was abraded so to penetrate the stratum corneum but not disturb the dermis. The Jojoba Esters 15 (0.5 ml) were applied to both sides of the exposed skin which were covered with a patch and polyethylene for 24 h. The sites were examined upon unwrapping and 48 h later. There was erythema for all the rabbits at the first reading and only 2 at the second reading but no edema formation. A score of ≥ 5 would indicate a positive irritant. The authors reported a mean score of 1.08.

Leberco Testing, Inc. (1988f) repeated the experiment with Jojoba Esters 30. There was erythema formation for all the rabbits at the first reading and only 2 at the second reading but no edema formation. A score of ≥ 5 would indicate a positive irritant. The authors reported a mean score of 0.42.

Leberco Testing, Inc. (1988g) repeated the experiment with Jojoba Esters 60. There was erythema formation for all the rabbits at the first reading and only 2 at the second reading but no edema formation. A score of ≥ 5 would indicate a positive irritant. The authors reported a mean score of 1.08.

Leberco Testing, Inc. (1988h) repeated the experiment with Jojoba Esters 70. There was erythema formation on 2 the rabbits at the first reading (1 on just intact skin and the other on both intact and abraded skin) and none at the second reading but no edema formation. A score of ≥ 5 would indicate a positive irritant. The authors reported a mean score of 0.17.

The skin irritation potential of 2 Jojoba Esters (iodine values = 40 and 60) was evaluated using 2 groups of 6 albino rabbits (ages not stated). Prior to application of the test substance, 10.0% of the body area of each animal was clipped free of hair. The test substance (0.5 ml) was applied to abraded and intact skin sites on the back. The Esters were applied as received. The application sites (abraded and intact) were covered with a 1 x 2 inch patch that was sealed with transparent tape. The entire treatment area was also wrapped with a sheet of polyethylene that was secured with tape. At 24 h post-application, the patches were removed and excess test material was wiped from each test site. Reactions were then scored at 24 and 72 h post-application according to the scales: 0 (no erythema) to 4 (severe erythema to eschar formation) and 0 (no edema) to 4 (severe edema). Primary irritation scores of 5 or greater were defined as positive skin irritation reactions. The mean primary irritation scores for the 2 esters were 0.42 and 1.08, respectively (Leberco Testing, Inc. 1988h).

Hydrolyzed Jojoba Esters

Celsis Laboratory Group (1999a) performed an in vitro Dermal Irritection test, which looks at changes in a biomembrane barrier to predict in vivo effects, on a sample of a mixture of Hydrolyzed Jojoba Esters and water (20:80 wt.%). The sample was found to be non-irritating at volumes of 25 to 125 µl. The researchers note that the pH of this sample was above the optimum range for the Irritection Assay System, thus there is a slight potential for irritation underestimation.

Simmondsia Chinensis (Jojoba) Butter

Brown (1984) evaluated the skin irritation potential of Jojobutter-51 using 6 male New Zealand white rabbits (2.3-3.0 kg). The test substance (0.5 ml, acid value = 2.8) was applied via gauze patches to abraded and intact sites (clipped free of hair) lateral to the midline of the back. The trunk of each animal was then wrapped with occlusive patches of polyethylene; patches and polyethylene coverings were secured with hypoallergenic tape for 24 h. Immediately after patch removal, excess test material was wiped from the skin with gauze. Reactions were scored at 24 and 72 h post-application according to the Draize scale: 0 (no erythema or edema) to 4 (severe erythema to slight eschar formation, and edema). At 24 h post-application, the following reactions were observed: no erythema (2 rabbits), very slight erythema (2 rabbits), and well-defined erythema (2 rabbits). Jojobutter-51 (acid value = 2.8) was classified as a mild irritant (Primary Irritation Index = 0.5). When samples of Jojobutter-51 with a reduced acid value (1.6) were applied to an additional 6 rabbits according to the same procedure, erythema was not observed. However, slight edema was observed at the abraded site of 1 rabbit at 24 h post-application. Jojobutter (acid value = 1.6) was classified as a nonirritant (Primary Irritation Index = 0.04).

Ocular Irritation

Simmondsia Chinensis (Jojoba) Seed Oil

The ocular irritation potential of refined Simmondsia Chinensis (Jojoba) Seed Oil was evaluated using 6 male white rabbits. Immediately after the oil (0.1 ml) was instilled into the conjunctival sac of the right eye of each animal, slight atretoblepharia was observed. Slight conjunctival hyperemia was observed 1 h after instillation. Ocular irritation did not increase in severity, and all reactions had cleared by 24 h post-instillation (Taguchi and Kunimoto 1977).

The ocular irritation potential of a lip balm product containing 20.0% Simmondsia Chinensis (Jojoba) Seed Oil was evaluated using 6 New Zealand white rabbits. The test substance (0.1 ml) was instilled once into the conjunctival sac of one eye. The untreated eye served as the control. Reactions were scored at 24, 48, and 72 h post-instillation according to the Draize scale. At 24 h post-instillation, the mean ocular irritation score was 0.3 ± 0.8. No reactions were observed at 48 and 72 h. The product was classified as a nonirritant (CTFA 1985c).

Simmondsia Chinensis (Jojoba) Seed Wax

Reinhardt and Brown (1990) evaluated the ocular irritation potential of Simmondsia Chinensis (Jojoba) Seed Wax in 6 albino rabbits (ages not stated). The only procedural variation was the instillation of 0.05 ml of test substance. The following reactions were observed in 3 of the 6 rabbits tested: conjunctival chemosis, obvious swelling with partial eversion of lids (1 rabbit), and conjunctival redness, diffuse crimson red conjunctiva in which individual vessels were not discernible (2 rabbits). As the test ingredient did not produce a positive reaction in 4 or more test animals, it was not classified as an eye irritant.

Hydrolyzed Jojoba Esters

Celsis Laboratory Group (1999b) reported that a mixture of Hydrolyzed Jojoba Esters and water (20:80 wt.%) was non-irritating in a chorioallantoic membrane vascular assay for possible eye irritation. No further details were provided.

Jojoba Esters

Leberco Testing, Inc. (1988i) administered Jojoba Esters 15 (0.1 ml) to the right conjunctival sac of albino rabbits (n = 6). The left eye served as the control. The eyes were examined at 24, 48, and 72 h. Four of the treated eyes showed redness of the conjuctivae at 24 h that was resolved by 48 h. The authors concluded that Jojoba Esters 15 did not produce a positive reaction in 4 or more of the test rabbits so the test material was not classified as an eye irritant.

Leberco Testing, Inc. (1988j) repeated the experiment with Jojoba Esters 30 (0.1 ml). One of the treated eyes showed redness of the conjuctivae at 24 h that was resolved by 48 h. The authors concluded that Jojoba Esters 30 did not produce a positive reaction in 4 or more of the test rabbits so the test material was not classified as an eye irritant.

Leberco Testing, Inc. (1988k) repeated the experiment with Jojoba Esters 60 (0.1 ml). Four of the treated eyes showed redness of the conjuctivae at 24 h that was resolved by 48 h. The authors concluded that Jojoba Esters 60 did not produce a positive reaction in 4 or more of the test rabbits so the test material was not classified as an eye irritant.

Leberco Testing, Inc. (1988l) repeated the experiment with Jojoba Esters 70 (0.05 ml). Two of the treated eyes showed redness of the conjuctivae at 24 h that was resolved by 48 h. One of the treated eyes exhibited chemosis (swelling above normal) at 24 h that was resolved at 48 h. The authors concluded that Jojoba Esters 70 did not produce a positive reaction in 4 or more of the test rabbits so the test material was not classified as an eye irritant.

The ocular irritation potential of 2 Jojoba esters (iodine values 40 and 60, respectively) was evaluated using 2 groups of 6 albino rabbits (ages not stated) (Reinhardt and Brown 1990). The test substance (0.1 ml) was instilled, as received, into the right eye of each animal. Untreated eyes served as controls. Reactions were scored at 24, 48, and 72 h post-instillation according to the following scales: corneal opacity scores of 0 (no ulceration or opacity) to 4 (complete corneal opacity, iris not discernible); scores for the iris of 0 (normal) to 2 (no reaction to light, hemorrhage, gross destruction; any or all of these); conjunctival redness scores of 0 (vessels normal) to 3 (diffuse, beefy red); conjunctival chemosis scores of 0 (no swelling of the lids and/or nictitating membrane) to 4 (swelling with lids more than half closed); conjunctival discharge scores of 0 (no discharge) to 3 (discharge with moistening of the lids and hairs, and considerable area around the eye). Test results were classified as positive only if 4 or more animals had positive reactions in the cornea, iris, and conjunctiva and negative if only 1 animal had positive reactions in the cornea, iris or conjunctiva.

Of the 2 groups of rabbits tested, 1 of 6 had a reaction to one of

the esters (iodine value = 60) and 4 of 6 had reactions to the other ester (iodine value = 30). All of the reactions were classified as conjunctival redness (diffuse, crimson red; individual vessels not easily discernable). As the test ingredient did not produce a positive reaction in 4 or more test animals, it would not be classified as an eye irritant (Reinhardt and Brown 1990).

Leberco Testing, Inc. (1994a) performed the Eytex test on a sample of Jojoba Esters 15. The test substance was rated minimal for irritation level at 20 to 100 µl.

Leberco Testing, Inc. (1995a) performed the Eytex test on a sample of Jojoba Esters 20. The test substance was rated minimal for irritation level at 10 to 100 µl.

Leberco Testing, Inc. (1994b) performed the Eytex test on a sample of Jojoba Esters 30 (dose not provided). The test substance was rated minimal for irritation level.

Jojoba Mixtures

Leberco.Celsis Testing (1997) tested for the possibility of ocular irritation by a mixture of isopropyl jojobate, Jojoba Alcohol, Jojoba Esters and tocopherol (approximate weight % 35:35:30:0.1) using the chorioallantoic membrane vascular assay. The mixture (100%; 40 µl) did not cause slight/moderate hemmorrage, capillary injection, ghost vessels, or other abnormalities in 6 eggs after 30 min of contact time. The researchers concluded that this mixture was nonirritating.

Jojoba Alcohol

The ocular irritation potential of 12.5%, 25.0%, and 50% Jojoba Alcohol (in refined Simmondsia Chinensis (Jojoba) Seed Oil) was evaluated using 3 groups of 3 rabbits, respectively, according to the procedure by Draize. The test substance (0.05 ml) was instilled into the conjunctival sac of the right eye of each animal, and the untreated left eye served as the control. There were no reactions in the cornea or iris in any of the animals tested. Reactions in the conjunctiva were observed, but not beyond 24 h post-instillation. At concentrations of 12.5% and 50.0% Jojoba Alcohol, conjunctival reactions decreased in severity from Draize scores of 1.3 to 0.7 and from Draize scores of 4.0 to 0.7, respectively, up to 24 h post-instillation. At a concentration of 25.0%, reactions with a Draize score of 2 persisted up to 6 h post-instillation (Taguchi no date).

Comedogenicity

Simmondsia Chinensis (Jojoba) Seed Wax

Bio-Technics Laboratories, Inc. (1990a) evaluated the comedogenicity of Simmondsia Chinensis (Jojoba) Seed Wax. The comedogenicity score was 2.67, classifying the test substance as moderately comedogenic.

Jojoba Esters

Bio-Technics Laboratories, Inc. (1990b) evaluated the comedogenicity of a Jojoba Ester (iodine value = 60) using 4 young adult New Zealand white rabbits. Three animals were treated with the test substance and 1 animal was treated with the positive control, isopropyl myristate. The test substance (5 ml) was added to 45 ml of mineral oil, and the solution was heated to a temperature of 70°C. Liberal applications of the test solution were made to the right external ear canal via a cotton-tipped applicator 5 days per week (once per day) for a total of 14 applications. After each application, the solution was rubbed into the skin with a glass rod. The untreated left ear served as the negative control. At the end of the application period, the animals were killed and treated and untreated external ears were removed, fixed in 10.0% buffered formalin, and evaluated histopathologically. Comedone formation was graded according to the scale: 0 (negative) to 5 (severe: widely dilated follicles filled with packed keratin, follicular epithelial hyperplasia causing partial or total involution of sebaceous glands and ducts; possible inflammatory changes). The test solution was noncomedogenic (score = 0), whereas, the positive control caused marked superficial acanthosis and hyperkeratosis.

Bio-Technics Laboratories, Inc. (1990c) evaluated another Jojoba Ester (iodine value = 40) according to the same procedure. The comedogenicity score was 0.65, classifying the test substance as between non-comedogenic and slightly comedogenic.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

No reproductive or developmental toxicity data were available.

GENOTOXICITY

Simmondsia Chinensis (Jojoba) Butter

The Ames test was used to evaluate the mutagenicity of 2 samples of Jojobutter-51 in strains TA97, TA98, TA100, and TA102 of *Salmonella typhimurium* (Marshall et al. 1983). The test substance (in tetrahydrofuran) was evaluated at concentrations ranging from 1 to 1000 µg/plate with and without metabolic activation. The concentration of rat liver homogenate used for metabolic activation in the bioassay was 84 µg protein per plate. Tetrahydrofuran served as the solvent control, and positive controls were as follows: sodium azide, 2-nitrofluorene, 9-aminoacridine, methyl methane sulfonate, and 2-aminofluorene. Jojobutter-51 was not mutagenic at any of the concentrations tested. All of the positive controls were mutagenic; the solvent control was not mutagenic. Jojobutter-51 also was not mutagenic in a second bioassay (same procedure and test concentrations) in which the concentration of rat liver homogenate was increased to 140 µg per plate, or in the absence of metabolic activation. With the exceptions of methyl methane sulfonate and 9-aminoacridine, results with negative and positive controls were similar to those reported in the first bioassay.

Jojoba Alcohol

The mutagenicity of Jojoba Alcohol was evaluated by Taguchi (no date) using *S. typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538 and *E. coli* strain WP-2 (uvr A). All strains were tested with concentrations of Jojoba Alcohol ranging from 1.25 to 40.0 nl/plate both with and without metabolic activation. Untreated cultures of each strain tested served as negative controls. The following chemicals served as positive controls: N-ethyl-N-nitro-N-nitrosoguanidine (strains TA100, TA1535, and WP-2 (uvr A) without activation), benzo(a)pyrene

(strains TA98, TA100, TA1537, and TA1538 with activation), 2-aminoanthracene (strain WP-2 (uvr A) with activation), 2-nitroflourene (strain TA 98 without activation), 9-aminoanthracene (strain TA1537 without activation), and 4-nitro-o-phenylenediamine (strain TA1538 without activation).

The highest numbers of revertants per plate, compared with controls, in each strain tested without activation were as follows: TA98 (1.5 x control, dose = 10 nl/plate), TA100 (1.2 x control, 10 nl/plate), TA1535 (2.7 x control, 20 nl/plate), TA1537 (1.4 x control, 40 nl/plate), TA1538 (1.8 x control, 20 nl/plate), and WP-2 (uvr A) (1.8 x control, 1.25 and 20 nl/plate). The highest numbers of revertants per plate, compared with controls, in each strain tested with activation were as follows: TA98 (1 x control, 2.5 nl/plate), TA100 (1 x control, 40 nl/plate), TA1535 (1 x control, 1.25 and 20 nl/plate), TA1537 (1.5 x control, 10 nl/plate), TA1538 (1.2 x control, 2.5 nl/plate), and WP-2 (uvr A) (1.2 x control, 5.0 and 40 nl/plate). In positive control cultures, the number of revertants per plate ranged from 3.2 to 41.7 times that of control cultures. The authors concluded that Jojoba Alcohol was not mutagenic (Taguchi no date).

Jojoba Mixture

Celsis Laboratory Group (1999c) conducted an Ames mutagenicity assay on a mixture of isopropyl jojobate, Jojoba Alcohol, Jojoba Esters, and tocopherol (35:35:30:0.1 wt%) on *S. typhimurium* (TA98, TA100, TA1535, TA1537, and TA1538) and *E. coli* (WP2). The positive controls with S9 used 2-aminoanthracine. Positive controls without S9 used 2-nitrofluorene for TA98 and TA1538, sodium azide for TA100 and TA1535, 9-aminoacridene for TA1537, and methyl methone sulfate for *E. coli*. For concentrations ranging from 1 to 100 mg/plate, there was no mutagenicity observed. There was no sign of toxicity.

CARCINOGENICITY

No carcinogenicity data were available.

CLINICAL ASSESSMENT OF SAFETY

Dermal Irritation and Sensitization

Simmondsia Chinensis (Jojoba) Seed Oil

Taguchi and Kunimoto (1977) evaluated the skin irritation potential of refined and crude Simmondsia Chinensis (Jojoba) Seed Oil using 26 patients (18-59 years old) with histories of eczema or dermatitis. Olive oil, safflower oil, and white petrolatum served as controls. The test substances were applied to the upper back for 48 h via adhesive bandages. Reactions were scored 30 min and 24 h after patch removal. Slight eczema, the only reaction reported, was observed in 1 of the patients patch tested with crude Simmondsia Chinensis (Jojoba) Seed Oil. This reaction was not observed 24 h after patch removal. In another skin irritation study (same procedure), both test substances and controls were applied to 20 patients (19-42 years old) with histories of eczema or dermatitis. Positive reactions to crude Simmondsia Chinensis (Jojoba) Seed Oil and olive oil (1 patient) were observed 30 min after patch removal. Positive reactions to refined Simmondsia Chinensis (Jojoba) Seed Oil, safflower oil, and white petrolatum (1 patient) were observed 30 min and 24 h after patch removal. Both patients were thought to have been inherently hyperallergic.

Scott and Scott (1982) tested a total of 6 patients who were suspected of being sensitive to Simmondsia Chinensis (Jojoba) Seed Oil in a contact dermatitis study. The patients were patch tested (muslin patches) with each of the following: (1) 20% Simmondsia Chinensis (Jojoba) Seed Oil mixed with 80% olive oil, (2) 20% Simmondsia Chinensis (Jojoba) Seed Oil mixed with 80% liquid petrolatum, (3) pure olive oil, (4) pure mineral oil, and (5) muslin only. Positive reactions (erythema or erythema and vesicles) to both Simmondsia Chinensis (Jojoba) Seed Oil mixtures were observed on the forearms of 5 patients within 24 or 48 h after patch application. None of the patients had reactions to olive oil, mineral oil, or muslin. When the patient with no reaction to Simmondsia Chinensis (Jojoba) Seed Oil mixtures subsequently used pure Simmondsia Chinensis (Jojoba) Seed Oil as a hairdressing, contact dermatitis of the scalp resulted. Reactions were not observed in a control group of 28 patients patch tested (muslin patches) with pure Simmondsia Chinensis (Jojoba) Seed Oil. These patients had no known sensitivities.

CTFA (1985d) submitted a clinical use test where a lip balm product containing 20.0% Simmondsia Chinensis (Jojoba) Seed Oil was applied to the lips of 200 adult female subjects daily for 4 days. The subjects were evaluated at baseline and at 2 and 4 weeks post-application for signs of subjective/objective irritation. No adverse reactions were noted at any time during the study.

CTFA (1985e) submitted a report where the skin irritation and sensitization potential of a lip balm product containing 20.0% Simmondsia Chinensis (Jojoba) Seed Oil was evaluated using 208 adult female subjects. The test substance (0.2 g) was applied for 24 h to the back of each subject, between the scapulae and waist (adjacent to the midline), via an occlusive patch. Applications were made 3 times per week for a total of 3 weeks. Patch removals on Tuesdays and Thursdays were followed by 24 h nontreatment periods, and those on Saturdays were followed by 48 h nontreatment periods. Reactions were scored prior to the next patch application according to the scale: 0 (no evidence of any effect) to 4 (deep red erythema with vesiculation or weeping). The application site was changed if a subject had a reaction of 2 (uniform, pink-red erythema) or greater during induction. If a 2+ reaction was observed at the new site, induction applications were discontinued. However, all subjects with induction reactions were patch-tested during the challenge phase. After a 10- to 19-day nontreatment period, a challenge patch was applied for 48 h to a new site. Reactions were scored at 48 and 72 h post-application. Mild, transient irritation, nonspecific in nature, was observed in 1 subject. The product was classified as a nonirritant and a nonsensitizer.

CTFA (1988) submitted a report where the skin irritation and sensitization potential of a topical oil product containing 0.5% Simmondsia Chinensis (Jojoba) Seed Oil was evaluated in the modified Draize-Shelanski repeat insult patch test using 152 normal subjects (38 males, 114 females; 18-65 years old). The

test substance (on occlusive patch) was applied to the upper back of each subject on Monday, Wednesday, and Friday for 3 consecutive weeks. Sites were scored 24 h after patch removal according to the scale: 0 (no reaction) to + + + + (bullae or extensive erosions involving at least 50% of the test area). After a 2-week nontreatment period, 2 challenge patches were applied consecutively to new sites (adjacent to old site) for 48 h. Sites were scored at 48 and 96 h. None of the subjects had allergic reactions. The product was neither a clinically significant irritant nor a sensitizer.

Hill Top Research, Inc. (1998b) performed a repeated insult patch test of Simmondsia Chinensis (Jojoba) Seed Oil. The test articles were 2 separate lots of Jojoba Oil (a yellow oil and a clear oil; 0.2 ml). They were repeatedly applied at 100% to the same site on the skin (site not specified) for 3 weeks to the subjects (100 men and women). After 2 weeks rest, the test articles were reapplied to different sites. The sites were read for sensitization at 48 and 96 h. One subject had a dermal response of grade 1 to both Oils at the 48-h observation which subsided by the 96-h observation. A second person had the same reaction to the clear Simmondsia Chinensis (Jojoba) Seed Oil which subsided by the 96-h observation. The researchers concluded that the Simmondsia Chinensis (Jojoba) Seed Oils showed no evidence of contact sentisization.

Consumer Product Testing Company (2003) conducted a repeated insult patch test of Simmondsia Chinensis (Jojoba) Seed Oil (100%) on 102 volunteers (males and females). The test material (0.2 ml) was applied to the upper back and covered by an absorbent pad held in place with a clear adhesive dressing (semi-occluded). Patches were applied 3 times/week for 3 weeks to the same location. Patches were removed by the volunteers 24 h after application and the test area was examined before each application for reaction. A challenge patch was applied 2 weeks after final induction patch to an area adjacent to the induction area. The patch was removed after 24 h and scored 24 and 72 h after application. All readings were negative throughout the test period. The authors concluded that Simmondsia Chinensis (Jojoba) Seed Oil does not have a potential for dermal irritation or allergic contact sensitization.

Hydrolyzed Jojoba Esters

International Research Services Inc. (2006) assessed the skin sensitization potential of a mixture of Hydrolyzed Jojoba Esters and water (20:80 wt.%). The test material (diluted to 10%) was applied to subjects (n = 104) Monday, Wednesday, and Friday for 8 applications. After a 10- to 14-day rest, the challenge patch was applied. The site was evaluated at 24 and 72 h. There were no adverse effects due to the test material. There was no evidence of sensitization. The researchers concluded that there was no evidence of potential clinical irritation under normal use conditions.

Jojoba Esters

Leberco Testing, Inc. (1995b) reported a repeated insult patch test of Jojoba Esters 70 (10% in mineral oil) to the upper back of subjects (n = 53) on Monday, Wednesday, and Friday for 3 weeks. The patches were left on for 24 h. After a 2-week rest, a new patch was applied to a new site on the upper back. After 24 h, the patch was removed and the site evaluated. The sites were evaluated again at 48 and 72 h. There were no reactions during the induction phase. One subject had a ± level reaction at the 24 and 48 h readings; it was resolved at the 72 h reading. The authors concluded that the sample of Jojoba Esters 70 demonstrated no potential for eliciting either dermal irritation or sensitization.

California Skin Research Institute (1997a) tested 4 Jojoba Esters (20, 30, 60, and 70) for irritation. The test materials (100%; 2 ml) were administered to the upper outer arm of the subjects (n = 15; ages 24 to 51 years) for 24 h under an occluded patch. The patch was removed and the test site observed at 15 min and 24 h after removal. There were no signs of irritant dermatittis.

Jojoba Alcohol

Taguchi (no date) evaluated the skin irritation potential of Jojoba Alcohol using 60 human subjects. Twenty subjects (healthy skin) were patch tested with 10.0 and 100.0% Jojoba Alcohol, and 40 subjects (contact dermatitis patients) were patch tested with 100.0% Jojoba Alcohol. Oleyl alcohol, at concentrations of 10.0% (normal subjects) and 100.0% (patients), served as the control. Patches containing the test substance were applied to the upper back for 48 h. Reactions were scored 30 min and 24 h after patch removal according to the scale: 0 to 4+. In the group of healthy subjects, one reaction (± reaction to 10.0% Jojoba Alcohol) was observed at 30 min; no reactions were observed at 24 h. There were no reactions to 100.0% Jojoba Alcohol in healthy subjects. In the group of patients, 1 reaction (± reaction to 100.0% Jojoba Alcohol) was observed at 30 min; no reactions were observed at 24 h. The reactions observed in the patient control group included one reaction (± reaction to 100.0% oleyl alcohol) at 30 min and no reactions at 24 h. There were no reactions to 10.0% oleyl alcohol in the healthy group of control subjects. Jojoba Alcohol was not a skin irritant.

Jojoba Mixtures

California Skin Research Institute (1997a) performed a test on a Jojoba product (a mixture of Jojoba Esters, isopropyl jojobate, and Jojoba Alcohol) for irritation. There were no signs of irritant dermatittis.

Hill Top Research, Inc. (1998a) performed a repeated insult patch test of a mixture of isopropyl jojobate, Jojoba Alcohol, Jojoba Esters and tocopherol (approximate weight % 35:35:30:0.1). The test substance (100%; amount not provided) was applied to the same site on the skin of subjects (n = 100; 18 years old or older) for ~3 weeks. After ~2 weeks rest, the test substance was applied to a new site on the skin. There were no adverse reactions reported during the course of this study.

Hill Top Research, Inc. (1998b) performed a repeated insult patch test of Jojoba Esters/Hydrogenated Jojoba Oil. The test article was one lot of Jojoba Esters/Hydrogenated Jojoba Oil (white crystals; 0.2 g). It was repeatedly applied at 100% to the same site on the skin (site not specified) for 3 weeks to the subjects (100 men and women). After 2 weeks rest, the test article was

reapplied to different sites. The sites were read for sensitization at 48 and 96 h. One subject had a dermal response of grade 1 to the Jojoba Esters/Hydrogenated Jojoba Oil at the 48-h observation which subsided by the 96-h observation. A second person had the same reaction to the Jojoba Esters/Hydrogenated Jojoba Oil at the 48-h observation both of which subsided by the 96-h observation. The researchers concluded that the Jojoba Esters showed no evidence of contact sentisization.

Phototoxicity

Simmondsia Chinensis (Jojoba) Seed Oil

CTFA (1985e) submitted a report where the phototoxicity of a lip balm product containing 20.0% Simmondsia Chinensis (Jojoba) Seed Oil was evaluated using 10 subjects. In half of the subjects, ~0.2 g of the test substance was applied for 24 h to the inner aspect of the right forearm, and, in the remaining half, to the inner aspect of the left forearm. Similarly, the nonirradiated control site was on the inner aspect of the right or left forearm. After patch removal, reactions were scored according to the scale: 0 (no evidence of any effect) to 4 (deep red erythema with vesiculation or weeping). The test sites were then irradiated for 15 min with UVA light (dose = 4,400 µW/cm2) at a distance of approximately 10 cm. In each subject, the nonirradiated control site was shielded with aluminum foil during irradiation of the test site. Reactions were scored at the end of exposure and 24 and 48 h later. None of the subjects had reactions, and the product was classified as nonphototoxic.

CTFA (1985f) submitted a report where a total of 102 female subjects (18-49 years old) participated in an outdoor use test. Each subject used a sunscreen oil containing 0.5% Simmondsia Chinensis (Jojoba) Seed Oil for 2 h (in sunlight) on 2 consecutive days. The subjects were evaluated at 24 and 48 h post-exposure. Three subjects experienced slight, transient discomfort that was considered to be clinically insignificant.

Jojoba Alcohol

Taguchi (no date) evaluated the phototoxicity of Jojoba Alcohol using 60 subjects. Twenty subject (healthy skin) were patch tested with 10.0% and 100.0% Jojoba Alcohol, and 40 subjects (contact dermatitis patients) were patch tested with 100.0% Jojoba Alcohol. Oleyl alcohol, at concentrations of 10.0% (normal subjects) and 100.0% (patients), served as the control. Patches containing the test substance were applied to the upper back for 48 h. Each test site was then irradiated with the minimal erythema dose of black light. Neither the duration of exposure nor the intensity of the light source was stated. Reactions were scored at 24 h intervals according to the scale 0 and 4+. The only reaction was a ± reaction observed in one of the patients. Reactions were not observed in any of the normal subjects. No reactions were observed at control sites that had been treated with oleyl alcohol. The authors concluded that Jojoba Alcohol was not phototoxic.

Jojoba Mixtures

California Skin Research Institute (1997b) performed a phototoxicity study on a mixture of isopropyl jojobate, Jojoba Alcohol, Jojoba Esters and tocopherol (approximate weight % 35:35:30:0.1). The test substance (100%; 0.2 ml) and the control (distilled water) were applied to the paraspinal region of the subjects (n = 17; age 23 to 60) for ~24 h. The test sites with the test substance were exposed to UV radiation (16 J/cm^2 UVA) at each subject's minimal erythema dose and the controls sites were protected from the radiation. Visual evaluations were performed on all test sites 1, 24, 48, and 72 h after patch removal. There were no adverse effects during this study. There was 1 erythematous reaction at the 48-h evaluation which resolved by the 72-h evaluation. The researchers concluded that the mixture did not exhibit significant phototoxicity potential when compared to the negative control.

SUMMARY

Photoallergenicity

Simmondsia Chinensis (Jojoba) Seed Oil

CTFA (1985e) submitted a study that evaluated the photoallergenicity of a lip balm product containing 20.0% Simmondsia Chinensis (Jojoba) Seed Oil using 30 subjects. For half of the subjects, approximately 0.2 g of the product was applied for 24 h to the inner aspect of the left arm, and for the remaining half, to the inner aspect of the right arm. Likewise, sites on the inner aspect of the right or left arm served as control (nonirradiated) sites. Each application was made via an occlusive patch on Mondays, Wednesdays, and Thursdays for a total of 9 induction applications. If irritation was not observed, all applications were made to the same site.

After patch removal, each site was subjected to non-erythemogenic ultraviolet radiation for 15 min at a distance of 10 cm from the source. The dosage of UVA light was approximately 4,400 µW/cm^2. Each non-irradiated control site was covered during irradiation of the opposite arm. Irradiated sites were scored immediately after patch removal and 24 h after UV light exposure (72 h after irradiation on Friday) according to the scale: 0 (no evidence of any effect) to 4 (deep red erythema with vesiculation or weeping). After a 13- to 18-d nontreatment period, a challenge patch was applied for 48 h to a new site, and reactions were scored after patch removal. The test site was then irradiated and scored 24 h later. No reactions were observed, and the product was classified as non-photoallergenic.

Case Reports

Wantke et al. (1996) reported on a case of a 44-yr-old woman who applied moisturizing cream to her face daily for at least 5 yr. For the 3 months before presentation she had itching a few hours after application. The past 2 weeks there was dermatitis on her face. She was patch tested with the standard European ointment series, the cream she was using, and a related cream by the same manufacturer. She tested negative for everything except the moisturizing cream she had been using. She was then patch tested with all of the individual ingredients of the cream; 20 controls (10 men, 10 women) were also tested for irritation. The woman tested positive for "Jojoba Oil" (1.5%, ++), myristyl lactate (0.5%) and maleated soybean oil (1.5%, +), maleated soy bean oil (1.5%) not deodorized (?+), and glyceryl stearate (4.9%) and polyoxyethylene 23-lauryl ether (+). There was only 1

questionable reaction to glyceryl stearate (4.9%) and polyoxyethylene 23-lauryl ether by 1 male in the control group. Contact with the company revealed that the formulation had been changed about 2 years prior to the patient's presentation and there were 2 other suspected cases of contact dermatitis due to the cream.

SUMMARY

This safety assessment of the cosmetic ingredients Simmondsia Chinensis (Jojoba) Seed Oil (originally Jojoba Oil) and Simmondsia Chinensis (Jojoba) Seed Wax (originally Jojoba Wax) also includes Hydrogenated Jojoba Oil, Hydrolyzed Jojoba Esters, Isomerized Jojoba Oil, Jojoba Esters, Simmondsia Chinensis (Jojoba) Butter, Jojoba Alcohol, and Synthetic Jojoba Oil. Jojoba products (except Synthetic Jojoba Oil) are based on the esters from the fixed oil expressed or extracted from seeds of the desert shrub, Jojoba, *Simmondsia chinensis*. Simmondsia Chinensis (Jojoba) Seed Oil is composed almost completely (97%) of wax esters of monounsaturated, straight-chain acids and alcohols with high-molecular weights (C16-C26). These wax esters exist principally (83%) as combinations of C20 and C22 unsaturated acids and alcohols. Simmondsia Chinensis (Jojoba) Seed Oil is stable and resists oxidation. The amount and composition of the oil expressed from *S. chinensis* seeds varies with maturity of the seeds and somewhat with location and climate conditions surrounding the plant.

Impurities include lead up to 0.8 ppm and arsenic up to 0.1 ppm.

Simmondsia Chinensis (Jojoba) Seed Oil in cosmetic products has increased from 188 in 1989 (in concentrations up to 25%) to 1123 uses in 2007 at up to 100%. Simmondsia Chinensis (Jojoba) Seed Wax had no uses listed in 1989 and is currently reported to be used in 8 cosmetic products at up to 2%. Hydrogenated Jojoba Oil is reported to be used in 71 cosmetic products, Jojoba Esters in 121 cosmetic products, Simmondsia Chinensis (Jojoba) Butter in 18 cosmetic products, Jojoba Alcohol in 21 cosmetic products, and Synthetic Jojoba Oil in 6 cosmetic products at up to 31%, 44%, 6%, 1%, and 0.1%, respectively. Hydrolyzed Jojoba Esters are in 86 cosmetic products up to 2%. Isomerized Jojoba Oil is not reported as being used.

Simmondisia Chinensis (Jojoba) Seed Oil was detected in the feces of mice fed the ingredient at 0.5 to 1.69 mg/10 g.

Simmondsia Chinensis (Jojoba) Seed Oil penetrated nude mouse skin. The main route of penetration was the hair follicle. Simmondsia Chinensis (Jojoba) Seed Oil in an emulsion with Brij 96 and Capmul in 40% water delivered Fluconazole through new born mouse skin at a greater rate than gel bases. Only a small amount of radio-labeled Simmondsia Chinensis (Jojoba) Seed Wax injected subcutaneously into albino mice was absorbed into carcass and the lipid fractions of the brain and liver. Following the injection of the radio-labeled Simmondsia Chinensis (Jojoba) Seed Wax in mice, the greatest counts of radioactivity were in the liver, brain, lungs, and carcass lipids.

Simmondsia Chinensis (Jojoba) Seed Oil altered the penetration of aminophylline and Diclofenac when applied in a microemulsion.

Weanling rats fed Simmondsia Chinensis (Jojoba) Seed Wax had reduced weight gain. Digestibility of the Wax was 41%. Fecal matter contained 51% fat when the rats were fed 12% Simmondsia Chinensis (Jojoba) Seed Wax. Efficiency of energy conversion was half that of the control diets.

Orally administered jojoba liquid wax to rats inhibited carrageenin-induced edema at 5 and 10 ml/kg. In a chick's embryo chorioallantoic membrane test, jojoba liquid wax reduced the granulation tissue weight by 15.8% and 38% at 30% and 50%, respectively, compared to controls. Ear edema induced by a croton oil/ethanol/pyridine/ethyl ether solvent was reduced by 28% and 43.6% at 30% and 50%, respectively, with less neutrophil infiltration and hyperemia compared to controls. Jojoba liquid wax injected at 5 and 10 ml/kg reduced NO levels by 31.4% and 32.8%, respectively, after the injection of sterile air then lippolysaccharides from *E. coli* compared to controls. Croton oil-induced myeloperoxidase activity of rats' ears was decreased by jojoba liquid wax at 30% and 50% by 29% and 53.3%, respectively.

Simmondsia Chinensis (Jojoba) Seed Oil increased blood cholesterol levels in rabbits fed a cholesterol-free diet. Rabbits fed a diet consisting of 1% cholesterol and 2% Simmondisa Chinensis (Jojoba) Seed Oil was 40% lower compared with controls.

Simmondsia Chinensis (Jojoba) Seed Oil inhibits hydroysis of vitamin A esters in chicks and rats.

When tested for acute toxicity, Simmondsia Chinensis (Jojoba) Seed Oil was not toxic to mice at 1.69 ml/10 g. Fewer than 50% of rats died when administered 21.5 ml/kg Simmondsia Chinensis (Jojoba) Seed Oil. The acute oral toxicity of a lip balm with 20.0% Simmondsia Chinensis (Jojoba) Seed Oil was greater than 5.0 g/kg. Simmondsia Chinensis (Jojoba) Seed Wax was not classified as a toxic substance in rats at 5.0 g/kg. Orally administered Jojoba Esters (15, 30, 60, 70) were not toxic to rats at 5 g/kg. Jojoba Esters (iodine values 40 and 60) were not toxic to white rats at 5.0 g/kg; the rats survived for 14 d after administration. Orally administered Jojoba Alcohol was not toxic to rats at 50 ml/kg.

Simmondisa Chinensis (Jojoba) Seed Oil administered in the diet of rats resulted in 10% mortality in all 3 exposures (1.0, 2.0, and 3.0 g/d). Simmondsia Chinensis (Jojoba) Seed Oil fed to rats reduced food consumption but did not affect food transit time. When rats in another study were fed up to 9% Simmondisa Chinensis (Jojoba) Seed Oil in their diet for up to 4 weeks, there were no deaths and no clinical signs. Lipid content in the feces and urea concentration increased dose-dependently. White blood cell counts increased in the high dose group.

Rats administered Simmondsia Chinensis (Jojoba) Seed Wax subcutaneously 6 d/week for 7 weeks at 1 ml/kg survived. Blood chemistry values were similar between controls and treatment groups. Simmondsia Chinensis (Jojoba) Seed Wax was not toxic when applied to the shaved backs of guinea pigs 6 d/week for 20 weeks up to 0.5 g/kg.

Simmondsia Chinensis (Jojoba) Seed Oil was not dermally

irritating when applied to guinea pigs at 0.5 ml for 15 d. When applied to intact and abraded skin of white rabbits in a lip balm at 20%, Simmondsia Chinensis (Jojoba) Seed Oil was minimally irritating with a mean score of 0.33 out of 4. Jojoba Esters (15, 30, 60, and 70) were not irritating to the intact and abraded skin of albino rabbits at 0.5 ml under an occluded patch for 24 h. When applied to the intact and abraded skin of albino rabbits, two Jojoba Esters (iodine values of 40 and 60) were non-irritating after 24 h under an occluded patch. Simmondsia Chinensis (Jojoba) Seed Wax was not irritating to albino rabbits. A Dermal Irritection test found Hydrolyzed Jojoba Esters and water (20:80 wt.%) to be non-irritating at 25 and 125 ml. Jojoba Alcohol was found to be non-irritating to the skin of albino marmots at 10.0% (in refined Simmondsia Chinensis (Jojoba) Seed Oil.

Simmondisa Chinensis (Jojoba) Butter was classified as a non-irritant when applied to the intact and abraded skin of New Zealand white rabbits at 0.5 ml for 24 h under an occluded patch. Jojoba Alcohol, up to 50% in refined Simmondsia Chinensis (Jojoba) Seed Oil, showed no signs of irritation at the macroscopic level when applied to the intact and abraded skin of white rabbits for 15 and 30 d. Microscopic evaluation revealed light to medium incrassation of the germinative zone of the epidermis and light dermal irritation. After 15 d, 25% Jojoba Alcohol induced redness, induration, and swelling. After 30 d, 25% Jojoba Alcohol induced redness; 50% induced redness, induration, and swelling. Histopathological examination was negative for other signs of irritation. The Draize test on albino marmots was negative at 10% Jojoba Alcohol, in refined Simmondsia Chinensis (Jojoba) Seed Oil.

Simmondsia Chinensis (Jojoba) Seed Oil was non- to slightly irritating when instilled into the eyes of white rabbits. Simmondsia Chinensis (Jojoba) Seed Wax was not classified as an ocular irritant when instilled into the eyes of white rabbits. Jojoba Esters (15, 30, 60, and 70) were not classified as ocular irritants when instilled into the eyes of albino rabbits. Jojoba Esters (iodine values of 40 and 60) were not classified as ocular irritants when instilled into the eyes of albino rabbits. In the Eytex test, Jojoba Esters (15, 20, and 30) were found to be non-irritating. Jojoba Esters in water (20:80 wt.%) was found to be non-irritating in a chorioallantoic membrane vascular assay. Jojoba Alcohol, at 12.5%, 25.5%, and 50% in refined Simmondsia Chinensis (Jojoba) Seed Oil, produced no reactions in the cornea or iris when instilled into the eyes of rabbits. Reactions in the conjuctivae did not last past 24 h. A mixture of isopropyl jojobate, Jojoba Alcohol, Jojoba Esters and tocopherol (35:35:30:0.1 wt.%) was found to be non-irritating in a chorioallantoic membrane vascular assay.

Simmondsia Chinensis (Jojoba) Seed Wax was moderately comedogenic, score 2.67. Jojoba Esters was noncomedogenic, when tested on white rabbits. Jojoba Esters were found to be non- to slightly- comedogenic in mineral oil.

Simmondsia Chinensis (Jojoba) Butter was found to non-mutagenic in an Ames test using *S. typhimurium* (strains TA97, TA98, TA100, and TA 102) up to 1000 mg/plate with and without metabolic activation. Jojoba Alcohol was found to be non-mutagenic using *S. typhimurium* (strains TA98, TA100, TA1535, and TA1537) and *E. coli* (strain WP-2) at 1.25 to 40.0 nl/plate, with and without metabolic activation. There was no mutgenicity observed in an Ames test of a mixture of isopropyl jojobate, Jojoba Alcohol, Jojoba Esters, and tocopherol (35:35:39:0.1 wt.%) using *S. typhimurium* (strains TA98, TA100, TA1535, TA153, and TA1538) and *E. coli* (strain WP-2).

One of 26 patients, all with a history of either eczema or dermatitis, had a slight eczema reaction to refined and crude Simmondsia Chinensis (Jojoba) Seed Oil after 24 h of exposure. When repeated with 20 more patients, there was 1 patient with a reaction after patch removal. There were no reactions among the control group. In a contact dermatitis study of 6 patients suspected of sensitivity to Simmondsia Chinensis (Jojoba) Seed Oil, 5 had positive reactions to 20% Simmondsia Chinensis (Jojoba) Seed Oil in olive oil and 20% Simmondsia Chinensis (Jojoba) Seed Oil in liquid petrolatum. When applied to the person with no reaction, pure Simmondsia Chinensis (Jojoba) Seed Oil as a hair dressing resulted in contact dermatitis of the scalp. There were no reactions among the control group.

A lip balm with 20% Simmondsia Chinensis (Jojoba) Seed Oil was applied to the lips of 200 adults for 4 d, there was no irritation observed. The skin irritation and sensitization potential of this lip balm was tested on the backs of healthy subjects. One subject in 208 had mild, transient irritation in a non-specific nature. There were no other reactions.

In a modified Draize-Shelanski repeat insult patch test of Simmondsia Chinensis (Jojoba) Seed Oil, there were no allergic reactions in 152 normal subjects.

In a repeated insult patch test of Jojoba Esters 70 (10% in mineral oil) applied to the backs of subjects 3 d/week for 3 weeks, did not produce a reaction during the induction phase. When reapplied 2 weeks later, 1 subject had a low level reaction at the 24 h reading.

Jojoba Esters (20, 30, 60, and 70) and a Jojoba mixture (Jojoba Esters, isopropyl jojobate, and Jojoba Alcohol) applied to 15 subjects produced no signs of irritant dermatitis. In a repeated insult patch test of a mixture of isopropyl jojobate, Jojoba Alcohol, Jojoba Esers and tocopherol (35:35:30:0.1 wt.%) on 100 subjects, there were no adverse reactions.

In a repeated insult patch test of Simmondsia Chinensis (Jojoba) Seed Oil (2 separate lots, yellow and clear) and Jojoba Esters/Hydrogenated Jojoba Oil on 100 subjects there was 1 grade 1 reaction to all 3 test substances at 48 h which resolved by the 96-h reading. One other person had a similar reaction to the clear Simmondsia Chinensis (Jojoba) Seed Oil and another to the Jojoba Esters/Hydrogenated Jojoba Oil. In a repeated insult patch test of Simmondsia Chinensis (Jojoba) Seed Oil at 100% on 100 subjects, there were no dermal reactions during course of the study.

In a skin sensitization test of Hydrolyzed Jojoba Esters in water (20:80 wt.%) diluted to 10% there were no reactions nor evidence of sensitization.

In a patch test of Jojoba Alcohol at 10.0% and 100.0% on 20 healthy patients and 40 contact dermatitis patients, there were no reactions in the healthy test group. In the dermatitis patients, there was 1 mild reaction to the 100.0% Jojoba Alcohol at the 30 min observation.

Lip balm containing 20.0% Simmondsia Chinensis (Jojoba) Seed Oil was applied to the forearms and irradiated with UVA for 15 min. There were no reactions and the lip balm was classified as non-phototoxic. Simmondsia Chinensis (Jojoba) Seed Oil in a sunscreen at 0.5% was administered to 102 subjects in sunlight for 2 consecutive days and found to be non-phototoxic. A mixture of isopropyl jojobate, Jojoba Alcohol, Jojoba Esters and tocopherol (35:35:30:0.1 wt.%) was found to be non-phototoxic at 100%. In a photoallergenicity test of a lip balm containing 20.0% Simmondsia Chinensis (Jojoba) Seed Oil on 30 subjects, the lip balm was applied and irradiated with UVA to the inner arm 3 d/week for 3 weeks. After a 13- to 18-day rest, the lip balm was reapplied for 48 h. There were no reactions observed and the product was classified as non-photoallergenic. Jojoba Alcohol, at 10.0% and 100.0%, applied to healthy patients and contact dermatitis patients and irradiated with UVA, resulted in 1 mild reaction in one of the dermatitis patients.

There was a case history of a woman who had itching dermatitis after using a moisturizing cream. Patch tests were negative for the ingredients in the cream except for "jojoba oil" and other ingredients.

DISCUSSION

The Cosmetic Ingredient Review Expert Panel noted that there were new uses listed in baby and eye products. Since the original safety assessment did not break down the categories of use to the extent that is now in practice, it was considered likely that Simmondsia Chinensis (Jojoba) Seed Oil and Wax were used in these products. Simmondsia Chinensis (Jojoba) Seed Oil is used up to 100% in bath products, which would be diluted when used, and in body and hand creams, etc., which would not be diluted. The Expert Panel considered, therefore, that exposure to 100% use concentration was possible.

In the absence of inhalation toxicity data, the Panel determined that Simmondsia Chinensis (Jojoba) Seed Oil, Hydrogenated Jojoba Oil, Jojoba Esters, and Jojoba Alcohol can be used safely in hair sprays, because the ingredient particle size is not respirable. The Panel reasoned that the particle size of aerosol hair sprays (~38 μm) and pump hair sprays (>80 μm) is large compared to respirable particulate sizes (≤10 μm).

The Expert Panel recognized that these ingredients can enhance the penetration of other ingredients through the skin (e.g. fluconazole and aminophylline). The Panel cautioned that care should be taken in formulating cosmetic products that may contain these ingredients in combination with any ingredients whose safety was based on their lack of dermal absorption data, or when dermal absorption was a concern.

Based on the composition of these ingredients, there were no structural alerts for reproductive/developmental toxicity and these ingredients are not expected to easily penetrate skin. None of the tested ingredients were genotoxic and there were no structural alerts for carcinogenicity. The Expert Panel expressed concern regarding pesticide residues and heavy metals that may be present in botanical ingredients, including Jojoba derivatives. They stressed that the cosmetic industry should continue to use the necessary procedures to limit these impurities in the ingredients before blending into cosmetic formulations. It was noted that the Synthetic Jojoba Oil was actually produced in the laboratory and not processed from the actual Simmondsia Chinensis (Jojoba) Seed Oil or Wax.

The CIR Expert Panel recognized that there are data gaps regarding use and concentration of these ingredients. However, the overall information available on the types of products in which these ingredients are used and at what concentrations indicate a pattern of use, which was considered by the Expert Panel in assessing safety.

CONCLUSION

Simmondsia Chinensis (Jojoba) Seed Oil, Simmondsia Chinensis (Jojoba) Seed Wax, Hydrogenated Jojoba Oil, Hydrolyzed Jojoba Esters, Isomerized Jojoba Oil, Jojoba Esters, Simmondsia Chinensis (Jojoba) Butter, Jojoba Alcohol, and Synthetic Jojoba Oil are safe as cosmetic ingredients in the practices of use and concentration as discussed in this safety assessment.[1]

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Bio-Technics Laboratories, Inc. 1990b. Comedogenicity study on Transjojoba-60, a jojoba ester. Unpublished data submitted by Jojoba Growers and Processors, Inc. 4 pages.[2]

[1] Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in the group.

[2]Available from the Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036.

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