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Non-comedogenic and hypoallergenic properties of jojoba oil and hydrogenated jojoba oil

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INTRODUCTION

Jojoba oil and its derivatives have found broad and growing application in cosmetic and personal care products. The jojoba plant (*Simmondsia chinensis*) is native to the Sonoran Desert that straddles the border of Mexico and the United States. Commercial plantations have been established in various suitable growing regions including Mexico, the United States, Argentina, Peru, and Israel. The oil from the seed of the jojoba plant is unique in that it is a pure liquid wax ester, not a triaclyglyceride typical of most seed lipids. Its composition is close to that of sperm whale oil, which was used abundantly in cosmetic formulations before being banned by various treaties protecting the whales' existence in the early 1970s.

Its chemical structure gives jojoba derivatives high stability and resistance to oxidation and degradation, enabling its storage for years in closed containers, in contrast to oils that become rancid and decompose with time. The liquid wax is composed of esters derived from C_{18}, C_{20}, C_{22}, and C_{24} monounsaturated acids and alcohols, as demonstrated in Figure 1 (1).

Hydrogenated jojoba oil retains the same structure, with the elimination of the double bonds (Figure 2). The fully hydrogenated wax esters form a hard white solid with a melting point of 69–70°C.

The history and the botanical, agrotechnical, and economic aspects of the plant and the wax are presented elsewhere (2). Although widely accepted for their non-occlusive properties, little clinical data to substantiate the effect(s) of these products on the skin exist. In this paper, the safety of jojoba oil and hydrogenated jojoba oil was investigated.

Draize and colleagues, in 1944, developed the Draize test for skin corrosivity and irritation using the rabbit skin and eye (3). Draize also developed early versions of an exaggerated patch test for irritation in humans. Later modifications by Maibach and Marzuli led over the years to the development of the so-called modified human Draize

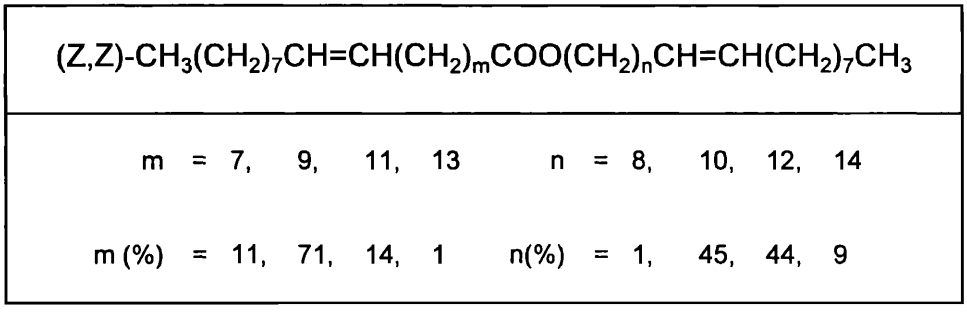

Figure 1. Jojoba oil structure.

patch test, or the human repeat insult patch test (HRIPT), to assess the contact sensitization potential of a material (4).

The development of a human follicular biopsy comedogenicity study, as developed by Mills and Kligman in 1981, provided a physiologically relevant test to assess comedone formation (5). Because African-American men have a greater propensity for comedones/acne, due to large pilosebacceous glands located in the upper back, they are often included in routine comedogenicity studies to exaggerate the potential for comedone formation of raw and/or finished product materials. Negative results in this particular population, when compared to the appropriate controls, provide a convincing set of data for non-comedogenicity claims.

To determine the safety of potential new products containing jojoba oil (both refined and pure), as well as hydrogenated jojoba oil, three preliminary studies were undertaken to evaluate their comedogenicity, and their phototoxic and allergenic potential(s).

MATERIALS AND METHODS

Two grades of jojoba oil, refined and pure, are available commercially. Both are expeller-pressed (mechanically extracted). The refined jojoba oil is filtered and refined with a dilute caustic to remove free fatty acids and hydratable phospholipids. The oil is bleached to remove all the color using a montmorilonite clay. Vacuum deodorization removes any remaining odors. Pasteurization is accomplished during the deodorization process. The pure jojoba oil receives only filtration and pasteurization, retaining the typical golden color and nutty aroma. Hydrogenated jojoba oil is produced by the nickel catalyzed hydrogenation of refined jojoba oil. The hydrogenated oil is bleached and deodorized. The physical properties of the materials are listed in Table I. Initially, these three substances were tested for cutaneous allergenic potential using the HRIPT, an adaptation of the Draize patch test (3,4).

HUMAN REPEAT INSULT PATCH TEST (HRIPT)

The purpose of the HRIPT was to evaluate the potential of one or more of jojoba test articles to induce allergic contact sensitization. Briefly, test articles were applied to the skin of the back utilizing a patch system under occlusive conditions in order to exaggerate exposure conditions. Each patch remained in place for approximately 48 hours

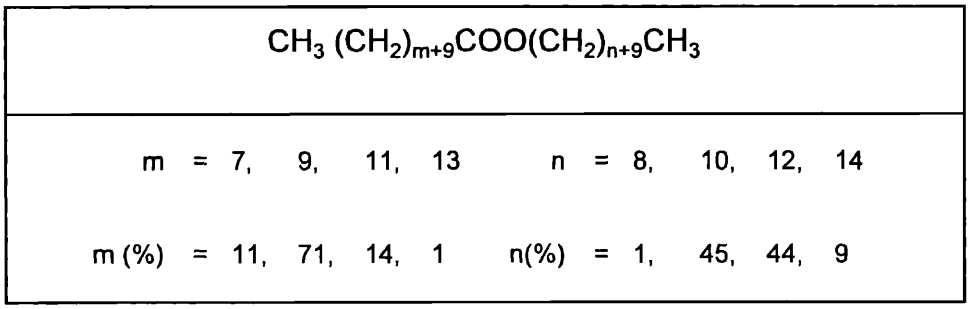

Figure 2. Hydrogenated jojoba oil structure.

Table I
Physical Properties

Analysis	Method (AOCS)	Refined jojoba oil (lot AJA-PN)	Pure jojoba oil (lot AJA-SR)	Hydrogenated jojoba oil (lot FEED25)
Acid value	Ci-4-91	0.055	0.38	0.5
Peroxide value	Cd-8b-90	Not detected	Not detected	0.1
Moisture content	Ca 2e-84 (Karl Fisher)	0.005%	0.013%	—
Color	Ce 13e-92 (Lovibond 5 1/4″)	<1 Y/0.1 R	59 Y/4.0 R	1 Y/0.4 R
Refractive index	Cc-7-25	1.4660 (22°C)	1.4655 (23°C)	—
Specific gravity	Cc-10a-25	0.864	0.865	—
Iodine value	Cd-1b-87	82.3	80.78	1.7
Saponification value	Cd-3-25	93.6	93	93

before being removed. Test sites were then evaluated and scored based on the degree of irritation and/or pre-sensitization, approximately 48 hours after patch applications (no evidence of pre-sensitization was seen). Following evaluation, the patch application and evaluation procedures were repeated until nine "inductions" occurred. After the ninth induction, subjects commenced the "rest period" of approximately two weeks, during which no applications of test material occurred. Immediately following the rest period, each of the test materials was applied to naïve skin sites for approximately 24 hours (termed "challenge" phase); evaluations and scores were performed approximately 48 and 96 hours after these patch applications.

PHOTOTOXICITY STUDY

This study was designed to evaluate the cutaneous phototoxic potential of the following test articles: pure and refined jojoba oil, hydrogenated jojoba oil, and distilled water (negative control).

A 150-watt solar ultraviolet simulator (Solar Light Co., Philadelphia, PA) provided the

ultraviolet radiation source in this study. The 1-mm WG-320 and 1-mm UG-11 was used to provide a basic solar-like spectrum (UVB: 290–320 nanometers; UVA: 320–400 nanometers). For pure UVA exposures, the UVB was removed with a 2-mm WG-345 filter allowing only solar-like UVA radiation exposures.

Only subjects with Fitzpatrick skin types I, II, and III were impaneled (6,7). Each subject's minimal erythema dose (MED) was estimated prior to patch applications. This was done by exposing five paraspinal test sites to UVB irradiation such that each test site received approximately 25% more total irradiation than the previous site. Visual evaluation approximately 24 hours later revealed the actual MED. Subjects' reactions were then allowed to resolve for at least 96 hours prior to continuing with the study. Each subject received one set of the four test articles, by patch application, to each of two paraspinal regions. Approximately 24 hours after the patch applications, patches within the left paraspinal region were removed. These test sites were exposed to 16 joules/cm^2 of UVA irradiation and approximately 0.75 MED of UVB irradiation, for a total administration of approximately one MED. Patches on the right paraspinal region were also removed at this time but were not irradiated. Visual evaluations were performed approximately 1, 24, 48, and 72 hours after removal of the patches.

COMEDOGENICITY STUDY

At the initial visit, one follicular biopsy was taken to assess each candidate's potential for comedone production. This method is a variation of the procedure published by Mills and Kligman (5). This procedure involves pressing a glass slide coated with two drops of methyl cyanoacrylate glue against the upper back to create an even layer of polymer. The glass slide is then gently peeled away, bringing with it any microcomedones. Study subjects must exhibit at least one microcomedone per 2-cm^2 area when viewed under a stereomicroscope to qualify as a panelist for the test.

Test articles and controls were administered to the suprascapular regions under occluded patch conditions. As a positive control, Acetulan was used; a blank patch served as the negative control. The patches were replaced with identical patches three times per week (Monday, Wednesday, and Friday) until a continuous exposure of 28 days was achieved. With each patch replacement, the test sites were cleansed with sterile water and allowed to air dry prior to application of the next patches. At the conclusion of the study, test sites (2 cm^2) were evaluated for microcomedones with one follicular biopsy at each test site.

RESULTS

HUMAN REPEAT INSULT PATCH TEST RESULTS

Healthy subjects, of age range 18–65 years, were impaneled in this study. Refined, pure, and hydrogenated jojoba oil provided no identifiable clinical evidence (e.g., erythema, edema) of contact sensitization. These results are summarized in Table II.

PHOTOTOXICITY STUDY RESULTS

Seventeen healthy subjects, of age range 23–60 years, completed the study. Under the

Table II
Summary of HRIPT Results

Test article	Results	Comments
Jojoba oil (lot AJA-PN)	1.01% (one subject) exhibited mild reaction (grade 1). All others showed no visible reaction (grade 0).	Dermal response of subject with mild reaction subsided to grade 0 at 96-hour assessment point.
Jojoba oil (lot AJA-SR)	2.04% (two subjects) exhibited mild reaction. All others showed no visible reaction.	Dermal response of subject 1 with mild reaction subsided to grade 0 at 96-hour assessment point. Dermal response of subject 2 exhibited a grade 1 dermal response at 96-hour assessment point.
Hydrogenated jojoba oil (lot FEED25)	2.04% (two subjects) exhibited mild reaction. All others showed no visible reaction.	Dermal response of both subjects with mild reaction subsided to grade 0 at 96-hour assessment point.

conditions of this study, refined, pure, and hydrogenated jojoba oil did not exhibit significant identifiable phototoxic potential when compared with the negative control. Table III summarizes these results.

COMEDOGENICITY STUDY RESULTS

Twenty five healthy subjects, of age range 18–60 years, were enrolled in this study. Following four weeks of exaggerated topical application with jojoba oil (both refined and

Table III
Summary of Phototoxicity Results

Test article	Results	Comments after 24 hours	Comments after 72 hours
Jojoba oil (lot AJA-PN)	11.76% (2 test sites) exhibited erythematous reaction at 48-hour evaluation.	0% non-irradiated test sites exhibited erythema beyond 24-hour evaluation.	Erythema of both sites resolved before 72-hour evaluation.
Jojoba oil (lot AJA-SR)	5.88% (1 test site) exhibited erythematous reaction at 48-hour evaluation.	0% non-irradiated test sites exhibited erythema beyond 24-hour evaluation.	Erythema of site resolved before 72-hour evaluation.
Hydrogenated jojoba oil (lot FEED25)	11.76% (2 test sites) exhibited erythematous reaction at 48-hour evaluation.	0% non-irradiated test sites exhibited erythema beyond 24-hour evaluation.	Erythema of both sites resolved before 72-hour evaluation.
Distilled water (negative control)	5.88% (1 test site) exhibited erythematous reaction at 48-hour evaluation.	0% non-irradiated test sites exhibited erythema beyond 24-hour evaluation.	1 test site inadvertently overexposed.

Table IV
Summary of Comedogenicity Results

Test article	No. microcomedones 2 cm^2 (mean)	p-Value vs positive control	p-Value vs negative control
Jojoba oil (lot AJA-PN)	2.40	0.002	0.640
Jojoba oil (lot AJA-SR)	1.84	0.005	0.280
Hydrogenated jojoba oil (lot FEED25)	2.08	0.0001	0.300
Acetulan (positive control)	5.32	—	0.007
Patch only (negative control)	2.72	0.007	—

pure) and hydrogenated jojoba oil, the average number of microcomedones per two-square-centimeter area was measured (Table IV). Results of the cyanoacrylate follicular biopsies revealed significantly less ($p < 0.05$) microcomedone formation in jojoba oil and hydrogenated jojoba oil treated areas versus the positive control, Acetulan. Refined, pure, and hydrogenated jojoba oils did not differ significantly in their capacity to induce microcomedone formation compared to the negative control.

DISCUSSION

Three different jojoba oil preparations were tested in three different skin assays. None of these substances showed signs of inducing identifiable contact sensitization nor were they comedogenic. In the test for photoxicity, infrequent, slight erythema was elicited in the UV-treated test sites, but these reactions were transient, with resolution in virtually all cases by 72 hours. Furthermore, significant irritation was not elicited within test sites not receiving irradiation, further supporting the results of the HRIPT.

Photosensitivity describes an abnormal or adverse cutaneous reaction to light energy (8). Photosensitizers can be administered either systemically or topically. Photosensitivity due to topical agents may be phototoxic, photoallergic, or a combination of the two. A combination of both types of reactions occurs frequently. Even though other methods have been reported for assessing the potential phototoxicity of given substances, the technique described by Kaidbey and Kligman was used here because of its sensitivity and specificity (9).

Techniques for testing the potential comedogenicity of a given product include animal models such as the rabbit ear (10). However, Frank has pointed out that no evidence exists that the rabbit ear model is predictive of acnegenicity in humans (11). Histology of the affected skin area demonstrating the follicular canal and its epithelium can also be used to assess comedogenicity, but this procedure is considerably more invasive and time-consuming than the follicular biopsy used in this study.

The results reported here suggest that the jojoba oils and hydrogenated jojoba oil tested in these studies may be useful in the preparation of future skin care products.

REFERENCES

(1) J. Wisniak, *The Chemistry and Technology of Jojoba Oil* (American Oil Chemists' Society, Champaign, IL, 1987), p. 43.

(2) A. Shanl, The struggles of jojoba, *Chemtech* (May 1995).
(3) J. H. Draize, G. Woodard, and H. O. Galvey, Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. *J. Pharmacol. Exp. Ther.,* **82,** 377–390 (1944).
(4) F. N. Marzuli, and H. I. Maibach, The use of graded concentrations in studying skin sensitizers: Experimental contact sensitization in man, *Food Cosmet. Toxicol.,* **12,** 219–227 (1974).
(5) O. H. Mills, and A. M. Kligman, A human model for assessing comedogenic substances, *Arch. Dermatol.,* **118,** 903 (1982).
(6) W. L. Billhimer, *Phototoxicity and Photoallergy in Clinical Safety and Efficacy Testing of Cosmetics,* W.C. Waggoner Ed. (Marcel Dekker, New York, 1990) pp. 43–74.
(7) K. H. Kaidbey and A. M. Kligman, Phototoxicity to a sunscreen ingredient, *Arch. Dermatol.,* 114, 547–549 (1978).
(8) J. P. Nater and A. C. DeGroot, *Unwanted Effects of Cosmetics and Drugs Used in Dermatology* (Elsevier, New York, 1985), pp. 109–110.
(9) K. H. Kaidbey, "Assessment of Topical Photosensitizers in Humans," in *Safety and Efficacy of Topical Drugs and Cosmetics,* A. M. Kligman and J. J. Leyden, Eds. (Grune & Stratton, New York, 1982), pp. 213–219.
(10) W. E. Morris and S. C. Dwan, Use of the rabbit ear model in evaluating the comedogenic potential of cosmetic ingredients, *J. Soc. Cosmet. Chem.* **34,** 215 (1970).
(11) S. B. Frank, Is the rabbit ear model, in its present state, prophetic of acnegenicity?, *J. Am. Acad. Dermatol.,* **6,** 3–373 (1982).