JOURNAL OF THE AMERICAN COLLEGE OF TOXICOLOGY
Volume 1, Number 4, 1982
Mary Ann Liebert, Inc., Publishers

Final Report on the Safety Assessment of Polybutene

Polybutenes are the isotactic polymers of isobutene and n-butene. Polybutenes provide viscosity or emulsifiability to more than 80 cosmetic products in concentrations up to 50%.

The results of acute oral and percutaneous toxicity tests of Polybutenes show these materials to be relatively harmless.

Acute skin irritation tests on rabbits showed no or mild irritation. Other test results indicate that Polybutenes are not toxic: (a) there were no observable effects in rats after inhalation at concentrations up to 18.5 mg/l of air; (b) there was only mild, transient eye irritation in rabbits; (c) intravaginal application of concentrated Polybutene daily for 30 days produced no observable effect in rabbits. Chronic oral toxicity in rats fed up to 20,000 ppm for three successive generations showed no impairment in reproduction.

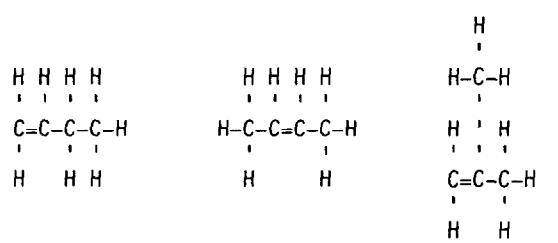
The available human clinical data indicated only very mild effects. Skin tests for sensitization, irritancy, phototoxicity, and photosensitization were limited to cosmetic formulations.

On the basis of the available information, it was concluded that Polybutenes are safe as presently used in cosmetics.

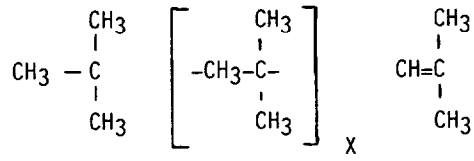
CHEMISTRY

Structure

POLYBUTENE is any one of several isotactic (stereoregular) polymers of isobutene and n-butene; the molecular weights of these polymers vary according to their degree of polymerization. Isobutene chains may contain from 10 to 100 subunits; n-butene monomers can be either 1-butene, 2-butene, or both.[1,2]



The olefin structure of Polybutene is predominantly the trisubstituted type ($R-CH=CR_2$). The major component of Polybutenes can be represented as:[3]



Other names include:[1,2,4] Butene, Homopolymer, Butene, Polymer, Polybutylene, Butene Polymer, Polyisobutylene, Poly (1-butene), and Poly-α-butylene.

Preparation

Passman[5] describes an industrial preparation of Polybutene in which a solution of 1-butene is dried and fed into a reaction chamber. A Zeigler-Natta reagent ($TiCl_3$ and diethyl aluminum chloride) is added to catalyze the polymerization process. The molecular weight of the end product is limited by the reaction temperature used in the chamber.

Properties

Polybutenes are light colored, nondrying, sticky, viscous liquids. They are stable when exposed to light, insoluble in water, and soluble in hydrocarbon and chlorinated hydrocarbon solvents. Polybutene-1 has a density of 0.92 g/cm^3 and a melting range of 124°C–130°C.[2,5,6]

Polybutene is available in a variety of grades. The differences depend on viscosity, which increases directly in proportion to increasing molecular weight.[7,8]

Polybutene films have a high resistance to stress cracking, and low stress deformation.[5]

Reactivity

Polybutenes undergo combustion, pyrolysis, and autoxidation; the latter two can occur during analytical treatment.[2,14,17] Their low polarity, low degree of unsaturation, and their closely packed, branched-chain molecular structure make Polybutenes resistant to chemical reaction.[6]

Analytical Methods

A number of methods for the analysis of Polybutene are available.

McCall and Falcone,[9] Zymonas,[10] and Corno[11] employed nuclear magnetic resonance (NMR) to identify Polybutene, and Mauzac[12] used it in a study tracing ^{13}C-labeled Polybutene. NMR deals with the measurements of energy gaps between states of different energy; this spectroscopic phenomenon requires the presence of an external magnetic field.[13]

Infrared (IR) spectroscopy, far-infrared spectroscopy, and Raman scattering are commonly used in Polybutene analysis. Stivala[14] employed IR methods to observe autoxidation of poly-1-butene, and Goldstein et al.[15] used the longer wavelength far-infrared spectroscopy in determining Polybutene. Using laser excitation, Cornell and Koenig[16] observed the Raman scattering spectrum of polybutene.

Chromatography methods are reported, including gas, gel-permeation, and thin-layer.[6,8,17-21] Thin-layer chromatography is widely employed in determining Polybutene residues on plants and in volatile plant oils.[6,8] Barton[19] describe a gas chromatographic determination of Polybutene which involves flash pyrolysis.

Differential thermal analysis and differential thermogravimetry were employed by Tiunova et al.[22] and Era and Jauhiainen,[23] respectively.

Impurities

A typical analysis of Polybutene contains isoparaffins (less than 5%), vinylidene and terminal

vinyl structures, chloride (20 to 100 ppm), sulfur-containing compounds [(as S) up to 50 ppm], and nitrogen compounds [(as N) up to 45 ppm].[3]

USE

Cosmetic Use

Polybutenes are used in more than 80 cosmetic formulations in concentrations ranging from one to >50% (Table 1).[24] The ingredient commonly adds to the viscosity of a formulation, or it may act as an emulsifier.[2]

Non-cosmetic Use

Polybutenes are components of lube-oil, microscope immersion oil, hot-melt adhesives, sealants, and cable insulation.[2,25,26] They are also used in or as fungicides, bird repellents, rodenticides, herbicides, insecticides and acaricides.[2,6-8,27-33]

BIOLOGICAL PROPERTIES

Polybutenes are used in agricultural sprays to control mildew, leaf mold, various fungi, phytophageous mites, insects, and weeds.[6,7,29,30,33-35] Polybutenes are primarily used as additives that provide complimentary activity to pesticides, as adhesives and as controlled release dispensers.[8,35] The pesticidal action is frequently mechanical trapping. Herne,[7] however, concluded that Polybutenes had a toxic effect on mites and that mechanical trapping was not the only mode of action involved; when applied in concentrations as little as 2.5% (by weight), various grades of Polybutene caused high mortality in mites. Bradbury and Fisher[29] report that the fungitoxic effect of Polybutene emulsions is solely the result of the activity of the emulsifier.

Briggs[36] observed that Polybutene sprays applied to peppermint plants caused premature aging of the leaves and low oil yield. He concluded that Polybutene was unsuitable as a pesticide for plants from which oils are extracted.

Animal Toxicology

Acute

Oral toxicity

The acute oral toxicity of Polybutene, as a single ingredient and in cosmetic formulations, was

TABLE 1. PRODUCT FORMULATION DATA.[a]

Ingredient	*Cosmetic product type*	*Concentration (percent)*	*Number of product formulations*
Polybutene	Eye shadow	>1–5	10
	Hair preparations (non-coloring)	>5–10	2
	Lipstick	>50	8
		>25–50	17
		>10–25	21
		>5–10	13
		>1–5	11
	Other makeup preparations	>10–25	1
	Moisturizing	>1–5	1
	Night	>10–25	1

[a]From Ref. 24.

tested using albino rats. Test methods and results are outlined in Table 2. Samples ranged in concentration from 3.7% to 75% and were delivered by oral intubation. The LD50s ranged from >5 to >50 g/kg and the Polybutene was considered to be relatively harmless. Mild lethargy and diarrhea occurred in some animals at high dosage levels; autopsy data revealed no abnormalities.

Percutaneous systemic toxicity

Test methods and results are noted in Table 3. The percutaneous systemic toxicity of Polybutene samples H-100 (viscosity 93.8 sec Saybolt at 210°F) and H-1500 (viscosity 15,000 sec Saybolt at 210°F), both 75% concentrate, was tested on four groups of four adult New Zealand strain albino rabbits (two male, two female for each dosage level). Twenty-four hours before the sample was applied, the backs of the animals were shaved free of fur to expose 10 percent of the total body area. Skin applications were made in four dosage levels of 3.04, 4.56, 6.83, and 10.25 g/kg (one dose level per group, per rabbit). The test material remained in contact with the skin for 24 h. After 24 h, exposure sites, mortality, and behavior were observed for 14 days. No abnormal behavioral reactions or deaths were noted at any dosage level. The acute percutaneous LD50 of H-100 and H-1500 Polybutene for the albino rabbits was >10.25 g/kg.[37,38]

The acute dermal systemic toxicity of a lipstick formulation containing 15% Polybutene was tested in 10 rabbits. The percutaneous LD50 of the lipstick was found to be greater than 2 g/kg (0.3 g/kg Polybutene) body weight.[39]

Skin irritation studies

Test methods and results are outlined in Table 4. The primary skin irritation of 15% Polybutene in a lipstick formulation was tested on six albino rabbits. The formulation was not a primary irritant; it had a Primary Irritation Index (PII) of 0.0.[40]

A sample containing 20% Polybutene was tested for acute skin irritation according to the Draize method. Six albino rabbits were used. A 0.5 g sample of the test material was applied under surgical gauze for 24 h to shaved intact and abraded skin. Intact skin showed erythema and eschar formation in all rabbits at 24 h; it persisted in two of six until 72 h. Edema occurred in the intact skin of three of six rabbits at 24 h, but cleared at 72 h. The abraded skin showed erythema and eschar formation in all animals through 72 h. Edema occurred in the abraded skin of five out of six animals at 24 h and persisted in three of six to 72 h. The primary skin irritation index was 1.29, indicating that this formulation was a mild irritant.[41]

An acute skin irritation study of a lipstick formulation containing 3.7% Polybutene was conducted according to the Draize method. Of the six rabbits tested, erythema and eschar formation occurred in the intact skin of two animals at 72 h, in the abraded skin of one at 24 h, and in the abraded skin of three at 72 h. Edema occurred in the abraded skin of one rabbit at 24 h and in two at 72 h. The primary skin irritation index was 0.38, and the formulation was considered to be nonirritating.[51]

The primary skin irritation of a product containing 44% Polybutene was tested according to a modification of the Draize method. A 0.5 ml dosage of the product was applied to the intact and abraded skin of six rabbits for three consecutive 24-hour periods. According to the Draize scores, Grade 1 erythema was seen in three of six rabbits on Days 1 and 2, and Grade 1 erythema was observed in two of six rabbits on Day 3. This product was considered to be mildly irritating.[52]

A modified Draize method was used to test a lip oil containing 30% Polybutene for primary skin irritation. Six rabbits were given 0.5 ml dosages for three consecutive 24-hour periods. The samples were applied to intact and abraded skin under open patch conditions. According to Draize scoring criteria, Grade 1 erythema occurred on two of six rabbits on Days 1 and 2 and in one of six on Day 3.[53]

Inhalation toxicity

A group of 10 Sprague-Dawley albino rats was exposed continuously for 4 h to an atmosphere containing an aerosol of a 5% aqueous emulsion of Polybutene (H-100). During the exposure period, the concentration of the test material was approximately 17.3 mg/L (expressed in terms of active ingredient). No deaths occurred and no abnormal behavioral reactions were noted.[54]

The same time exposure was used to test the acute inhalation toxicity of an atmosphere containing

TABLE 2. ORAL TOXICITY.

No. of rats	*Conc. (Percent)*	*Dose/kg*	*Route*	*Study time (Days)*	*LD50/kg*	*Comments*	*Ref.*
Acute							
10	15	–	Oral intubation	–	>5.0 g	Nontoxic, Lipstick product	42
6	24	0.0 ml	Oral intubation	14			43
18	24	20.0–40.0 ml	Oral intubation	14	>40.0 ml	Mild lethargy for 24 h following intubation	
24	30	10.0–40.0 ml	Oral intubation	14	>40.0 ml	One death at 10.0 ml/kg at 24 h	44
10	30	50.0 ml	Oral intubation	–	>50.0 ml	No deaths. Mild diarrhea for 72 h. Lip product.	45
10	44	20.0 ml	Oral intubation	–	>20.0 ml	No abnormalities. Lip product.	46
16 albino	75	10.3–34.6 g	Oral intubation	14	>34.6 g	No deaths or abnormal behavior Polybutene H-100	47
16 albino	75	10.3–34.6 g	Oral intubation	14	>34.6 g	No deaths or abnormal behavior Polybutene H-1500	48
20	[a]	5.0–40.0 g	Oral intubation	7	>40.0 g	No deaths. Lip product.	49
20	[b]	5.0–40.0 g	Oral intubation	7	>40.0 g	One death at 40.0 g/kg level on Day 1. Lip product.	50

[a]20% in product. Product administered as a 50% solution in corn oil.
[b]3.7% in product. Product administered as a 50% solution in corn oil.

TABLE 3. ANIMAL TOXICOLOGY PERCUTANEOUS SYSTEMIC TOXICITY.

No. or rabbits	*Conc. (Percent)*	*Dose/kg*	*Route*	*Study time (Days)*	*LD50/kg*	*Comments*	*Ref.*
Acute							
16 albino	75	3.0–10.3 g	Shaved back	14	>10.3 g	No deaths or abnormal reactions. Polybutene H-100	37, 38
10 rabbits	15	2 g (of product)	–	–	>2.0 g	15% in formulation	39

18.5 mg/L of Polybutene (H-1500) on 10 Sprague-Dawley rats. Neither behavioral changes nor deaths occurred among the exposed rats.[55]

Eye irritation

Test methods and results are listed in Table 5. A group of five albino New Zealand rabbits was used to evaluate the eye irritation of undiluted Polybutene H-100 (75% concentration). This test was patterned after the Draize method, in which 0.1 ml of the test material was instilled into the conjunctival sac of the right eye of each animal while the left eye serves as a control. The Draize scoring system was used to grade irritation at 1, 24, 48, 72, and 96 h and 7 days after instillation. A zero score indicates no irritation; a score of 110 shows maximal irritation and tissue damage. In four rabbits, mild irritation (average score of 3.8) persisted to 48 h, after which time all irritation cleared for the remainder of the seven-day observation.[56]

Undiluted Polybutene H-1500 (75% concentration) was tested according to the Draize method for ocular irritation in a group of five albino rabbits. The product produced mild irritation in all animals at 24 h (average score 11.4), in four of the five animals at 48 h (score 7.4), and in three of them at 72 h (score 5.6). After 72 h, the eyes remained free of irritation for the rest of the seven day observation.[57]

A lipstick formulation containing 15% Polybutene caused no ocular toxicity in six rabbits after 24-, 48-, or 72-hour intervals.[58]

A red lipstick paste containing 20% Polybutene was tested for ocular irritation in six rabbits. A dose of 0.1 g/ml of the test materials was instilled with no washout into the right eye of three of the animals. Observations were made after Days 1, 2, 3, and 7. In the second group, the test material was instilled into the eye with a washout four seconds later. All rabbits were observed on Days 1, 2, 3, and 7. All animals in the first group developed conjunctival effects which cleared during the seven-day period. Their average Draize scores after 24, 48, and 72 h were 3.3, 2.0, and 1.6, respectively. The rabbits in the second group displayed conjunctival effects which disappeared at 48 h. Their average Draize scores for the same time intervals were 3.3, 0.0, and 0.0, respectively. The material was found to be a mild, transient irritant both when it was washed out and when it was not.[59]

A sample of 24% Polybutene was tested on nine albino rabbits in a Modified Draize Eye Irritation Study. A 0.1 ml sample of the substance was instilled into the right eye, and observations were made at 24, 48, and 72 h, and seven and 14 days. The six rabbits with unwashed eyes had an average Draize score of 0.222 out of a possible 110. The three rabbits with eyes washed immediately following instillation had an irritation score of 0.0. Thus, the substance was nonirritating.[60]

A lip product containing 55.2% Polybutene was tested for ocular irritation on six New Zealand rabbits. This product caused no irritation.[61]

Another lip product containing 44.0% Polybutene was tested by the Federal Hazardous Substances Act (FHSA) method on six rabbits. When a 0.1 sample of the product was instilled into the eye without a washout, no irritation resulted.[62]

A third lip product containing 30% Polybutene was tested according to the FHSA method on six rabbits. A 0.1 ml sample was instilled into the left eye, and no washout followed. At 24 h, mild conjunctivitis was observed in all six animals; all eyes were clear at 72 h. The product was considered nonirritating.[63]

Subchronic

Dermal systemic toxicity

The effect of Polybutene on hepatic drug-metabolizing enzymes and on skin benzo(a)pyrene hydroxylase was studied in rats. The Polybutene was applied to rat skin in a 10 μl volume (dissolved in mineral oil) daily for six days. It did not affect liver weight, microsomal protein, cytochrome P-450 or drug metabolizing enzyme activity of the liver. Similarly, it did not affect hepatic or skin enzymatic activities.[26]

Mucous Membrane Irritation

Undiluted Polybutene was applied to 12 female New Zealand white rabbits to study its subchronic mucous membrane irritation potential. Six of the rabbits were injected intravaginally daily for 30

TABLE 4. SKIN IRRITATION.

No. of rabbits	*Conc. (Percent)*	*Dose/kg*	*Route*	*Comments*	*Ref.*
Acute					
6 albino	15	–	–	– PII = 0.0 in a formulation	40
6 albino	20	0.5 g	Shaved intact and abraded skin	72 h PII = 1.29	41
6 albino	3.7	0.5 g	Shaved intact and abraded skin	72 h PII = 0.38	51
6 albino	44	0.5 ml	Shaved intact and abraded skin	Grade 1 erythema in 3/6 rabbits on Day 2; in 2/6 on day 3. Mildly irritating.	52
6 albino	30	0.5 ml	Shaved intact and abraded skin	Grade 1 erythema in 2/6 on Day 2; in 1/6 on Day 3.	53

TABLE 5. ANIMAL TOXICOLOGY EYE IRRITATION.

No. of rabbits	*Conc. (Percent)*	*Dose (ml)*	*Route*	*Study time (Days)*	*Comments*	*Ref.*
Acute						
5 albino	75	0.1	Eye instillation	7	Draize score at 48 h = 3.8 Polybutene H-100	56
5 albino	75	0.1	Eye instillation	7	24 h score–11.4; 48 h score–7.4; 72 h score–5.6 Polybutene H-1500	57
					Product Formulation	
6	15	–	Eye instillation	3	No ocular toxicity, 15%	58
6	20	0.1	Eye instillation	7	Unwashed eyes–24, 48, 72 h score = 3.3, 2.0, 1.6 Washed eyes–24, 48, 72 h score = 3.3, 0.0, 0.0	59
9	24	0.1	Eye instillation	14	Unwashed eyes–Draize score = 0.222 Washed eyes–Draize score = 0.0	60
6	55.2	–	Eye instillation	–	No irritation	61
6	44.0	0.1	Eye instillation	–	No irritation	62
6	30.0	0.1	Eye instillation	3	Nonirritating	63

consecutive days with 0.2 cc (0.2 ml/kg) of Polybutene. The other six were injected with saline as a control. The test compound produced neither signs of systemic toxicity nor behavioral changes, and all vaginas appeared normal.[64]

Chronic

Oral toxicity

Some of the test methods and the results are listed in Table 6. A two-year chronic oral toxicity study of Polybutene (H-100) (75% concentrate) was conducted on 240 Charles River albino rats. The animals were divided into four groups, each group being comprised of 30 males and 30 females. They were given 0 (control), 800 (0.08%), 4000 (0.40%), or 20,000 (2.0%) ppm Polybutene blended in their basic diets. The rats were checked for body weights, mortality and reactions, tumor incidence, and hematologic, urologic and pathologic changes. After 12 months of testing, five animals from each group were sacrificed for examination; no gross or microscopic pathological changes could be correlated with Polybutene ingestion. After 24 months of feeding, no significant differences were found in body weights or weight of food consumption, hematological results, urology, or tumor formation between the animals fed Polybutene and those that were not.

In the 20,000 (2.0%) ppm group, three of six males that died between weeks 17 and 24 exhibited hematuria. One other male in this group exhibited similar reactions, but completely recovered within two weeks; necropsy of the three rats revealed that two had clotted blood in the urinary tract, bladder, stomach, and intestines. The third animal revealed no significant gross pathologic changes. No abnormal reactions were noted in any other tested animal.[65]

A two-year chronic oral toxicity study of Polybutene H-100 (75% concentrate) was conducted on beagle dogs. The substance was administered orally daily to three test groups, each consisting of eight pure-bred beagle hounds (four male, four female). Each group was given one of the following doses: 40, 200, and 1000 mg/kg of body weight, or 0.045, 0.227, and 1.14 ml of test material. An untreated control group consisted of 5 male and 2 female dogs. Complete hematologic studies, blood chemistry, urinalysis, and liver function tests were conducted on the control and the highest dosage group after 90, 180, and 540 days of testing, and on all four groups after 360 and 720 days of testing. After one year of testing, one male and one female from each test group were sacrificed. At two years, all surviving dogs from all groups were sacrificed and major tissues and organs were examined. This study found that daily oral administration of Polybutene H-100 to pure-bred beagle dogs over a two-year period at the specified dosages caused no abnormalities in body weight, food consumption, survival, behavioral patterns, hematology, blood chemistry, urinalysis, liver function, gross and histopathologic examinations, or organ weights and ratios.[66]

Teratogenicity

Polybutene fed to rats at 1% or 10% in the diet for six months did not affect body weight gain, fertility, or gland weight. There were no teratogenic effects.[67]

Reproduction studies

A three-generation reproduction study was conducted on albino rats to determine the effect of ingesting Polybutene H-100. Three groups of Charles River albino rats (eight males and 16 females per group) were fed Polybutene in the following three dosage levels in the diet: 0 ppm (control), 800 ppm, and 20,000 ppm. Results showed that except for the test (F_2) male parental animals that were fed 20,000 ppm Polybutene, none of the animals in successive generations differed from controls with regard to weight gains. The F_2 male parental animals showed slight weight depression, although their growth patterns were still within the normal range. Differences in mortality or reaction or in gross or microscopic histology could not be correlated with the ingestion of Polybutene. Organ weight and ratio data revealed a few intergroup diffrences which were considered "random effects."

Reproductive performances (mating indices, fertility indices, incidence of pregnancy and parturition, and gestation times) of control and test animals were essentially comparable. Lactation indices ranged from 83% to 94% in the control group and from 89% to 99% in the 20,000 ppm group. In all three generations, there were no significant differences between test and control animals with regard to litter size, the number of stillborn, and the number of viable pups during lactation. The survival, body weights, and reactions of test animals were comparable to those of controls.[68]

TABLE 6. CHRONIC ORAL TOXICITY.

No. and species of animals	*Dose/kg*	*Route*	*Study time*	*Comments*	*Ref.*
Chronic					
				Polybutene H-100	
240 albino rats	0–20,000 ppm	Diet	2 years	3 deaths in 20,000 ppm group No other abnormalities	65
				Polybutene H-100	
6 beagles	Control 0.0 ppm				
24 beagles	40–1,000 ppm or 45–1.14 ml	Diet	2 years	No abnormalities	66
Rats		1.0% in diet	6 months	No teratogenic effects	67
Rats		1.0% in diet	6 months		

Human Clinical Studies

Primary Skin Irritation

The primary irritation potential of a lipstick formulation containing 20% Polybutene was patch-tested on 100 women. The entire upper back of each panelist was thoroughly cleansed with 70% isopropyl alcohol. The formulation was impregnated into one-half inch square blotting paper, applied to the skin and then covered with Patchplaster. After remaining in contact with the skin for 48 h, the paper was removed from the skin. Observations for reactions were made immediately, fifteen minutes later, and at 24 and 48 h. No inflammatory reactions occurred.[69]

The primary irritation potential of a lipstick formulation containing Polybutene (concentration unspecified) was tested on 100 women. Their backs were thoroughly cleansed with alcohol before application of the material. A closed one-half inch square patch was applied to the backs for 48 hours. The test sites were observed at 48 and 72 h after removal of the patches for reactions. No evidence of any inflammatory reaction on the site appeared at any of the observation periods.[70]

Repeated Insult Patch Tests

Test methods and results are listed in Table 7. A lipstick containing 15% Polybutene was tested for irritation by the Schwartz-Peck Prophetic Patch Test. There were "virtually" no reactions in the 195 subjects.[71] When the Draize-Shelanski Repeated Insult Patch Test was used to evaluate this same formulation on 96 subjects, there were "virtually" no reactions.[72]

A Modified Draize-Shelanski Repeated Insult Patch Test was used to determine the potential for irritation and sensitization caused by a lip lotion containing 30% Polybutene. The materials were applied to 50 human volunteers on the same patch sites for one 72-hour period and then for eight alternate 24-hour periods. After a 12-day rest period, challenge 48-hour patches were applied to the same sites on all subjects. Observations were made upon removal of the patch, and challenge sites were read 24 h after patch removal. The product caused neither sensitivity nor significant irritation.[73]

Another lip lotion formulation containing 30% Polybutene was tested according to the protocol just described. In the Modified Draize-Shelanski Repeated Insult Patch Test, the 50 volunteers showed neither sensitivity nor irritation.[74]

A lip lotion containing 24% Polybutene was tested for irritation and allergenicity according to the Modified Draize-Shelanski-Jordan Patch Test. The test material was applied to the upper backs of 50 volunteers for 48 h and then reapplied for 10 alternate 24-hour periods; readings were made at 48 h. After a 13-day rest period, a 48-hour challenge patch was applied, and a second 48-hour patch was applied seven days later. The challenge sites were read 48 and 72 h after application. Neither sensitization nor irritation was observed.[75]

A repeated insult patch test was conducted on a lip gloss containing 3.1% Polybutene in order to assess its irritation and allergic sensitization potential. An application of the material was made under occlusion every 48 h to the 104 panelists until there was a total of 10 applications per site. The site was graded for irritation 15 min after removal of the patch after each 48-hour application. After an 11-day rest period, a challenge patch was applied for 48 h. The site was graded 15 min and 24 h after removal of the patch. Two of the 104 panelists showed positive reactions of unspecified type. The product was considered to show no evidence of irritation or allergic sensitization.[76]

A repeated insult patch test according to the Draize-Shelanski-Jordan Procedure was conducted on a formulation containing 15.5-18.2% Polybutene. Of the 4717 subjects tested, six showed a Grade 1 Draize reaction.[77]

Lip gloss products containing 43.8-44.0% Polybutene were tested in the manner described above. Of the 2545 subjects, two showed a Grade 1 Draize reaction.[77]

Lip products with a 30.0% Polybutene concentration were tested according to the Draize-Shelanski-Jordan Procedure. Of the 7279 subjects who were tested, one showed a Grade 1 Draize reaction.[77]

A Draize-Shelanski-Jordan test of a lip product containing 50% Polybutene caused no irritation in 198 subjects.[77]

In a four-week controled use test, four formulations were tested for irritation potential. A lip gloss

TABLE 7. HUMAN CLINICAL STUDIES.

No. of subjects	*Conc. (Percent)*	*Dose*	*Time*	*Comments*	*Ref.*
Primary Skin Irritation				Product formulations	
100	20	—	48 h contact 3-day observe	No reactions	69
100	—	—	48 h contact 3-day observe	No reactions	70
Repeated Insult					
195	15	—	—	No reactions	71
96	15	—	—	No reactions	72
50	30	—	—	Material applied for one 72 h period; then, eight alternate 24 h periods Caused no irritation or sensitivity	73
50	30	—	—	Same protocol as above Caused no irritation or sensitivity	74
50	24	—	—	Applied for one 48 h period and then for 10 alternate 24 h periods; 13-day rest, then 48 h challenge No irritation or sensitization	75
104	3.1	—	—	Ten 48 h applications; 11-day rest; 48 h challenge patch No irritation or sensitization	76
4717	15.5–18.2	—	—	6/4717 showed Grade 1 Draize reaction	77
2545	43.81–44.0	—	—	2/2545—Grade 1 Draize reaction	77
7279	30.0	—	—	1/7279—Grade 1 Draize reaction	77
198	50.0	—	—	No irritation	77
407	15.5–18.2	—	4 weeks	1/407 showed erythema	78
219	43.81–44.03	—	4 weeks	No reactions	78
817	30.0	—	4 weeks	No reactions	78
25	50.0	—	4 weeks	1/25—blister on lower lip	78
63	15.0	—	28 days	Applications 2 × a day for 28 days. No irritation or sensitization.	79
Phototoxicity					
280	15.8–18.2	—	—	No reactions	80
165	43.81–44.02	—	—	No reactions	80
448	30.0	—	—	No reactions	80
27	50.0	—	—	No reactions	80

product containing 15.5–18.2% Polybutene was tested in 407 individuals. One erythematous reaction occurred. When lip formulations containing 43.8–44.0% Polybutene and 30.0% Polybutene were tested on 219 and 817 subjects, respectively, they produced no irritation. A lip product containing 50% Polybutene was applied to 25 panelists. A blister appeared on the lip of one person. No other reactions occurred.[78]

Sixty-three women panelists applied a lip formulation containing 15 percent Polybutene to test for product-induced irritation. The product was applied to the lips twice a day for 28 days, and the panelists were examined at 0-, 1-, 2-, 3-, and 4-week intervals. The panelists did not exhibit any irritation or sensitization.[79]

Phototoxicity and Photoallergenicity

Three lip gloss formulations, Type A (15.8–18.2% Polybutene), Type B (43.81–44.02% Polybutene), and Type C (30.0% Polybutene) were photopatch tested for phototoxicity and photoallergenicity in 280, 165, and 448 persons, respectively. A Xenon Arc Solar Simulator (150 W), which produces continuous emission spectrum from 290 to 400 nanometers, was used. These three products produced no reactions.[80]

A lip conditioner containing 50.0% Polybutene, tested on 27 individuals, did not induce any reactions.[80]

SUMMARY

Polybutenes are stereoregular polymers of isobutene and n-butene. The polymer chains may contain from 10 to 100 subunits and are prepared by heating 1-butene with catalysts. Polybutenes are light colored, nondrying, sticky, viscous liquids which are stable to light and soluble in hydrocarbon solvents. They undergo combustion, pyrolysis, and autoxidation. Analytical methods include nuclear magnetic resonance spectroscopy (NMR), infrared, far-infrared, and Raman scattering spectroscopy, and gas, gel, and thin layer chromatography. Impurities of Polybutene include isoparaffins, vinylidene, terminal vinyl structures, chloride, and sulfur containing compounds. Polybutenes are used in over 80 cosmetic formulations in concentrations ranging from 1 to >50%. They serve as viscosizers and emulsifiers.

When tested for acute oral toxicity in albino rats, concentrations of Polybutene ranging from 15% to 75% were relatively harmless. In percutaneous systemic dermal toxicity tests and in primary skin irritation studies, Polybutene in formulations produced no abnormalities or irritation in rabbits. Polybutene produced no abnormalities in rats during a 18.5 mg/L inhalation exposure and rabbits suffered only minimal eye irritation when Polybutenes were instilled into the eyes with and without washouts. In subchronic dermal systemic toxicity studies, Polybutenes did not affect hepatic or skin enzymatic activities in rats. It produced no irritation or signs of systemic toxicity when applied to the vaginas of rabbits. Chronic oral toxicity studies of up to 20,000 ppm Polybutene in the diet of rats and up to 1000 mg/kg daily in dogs for two years produced no adverse effects, and no teratogenic effects were found when fed to rats at 1% or 10% in the diet for six months. In three-generation reproductive studies with rats, Polybutene-fed rats showed no significant deviations from the control rats in any generation. Human primary irritation tests of a formulation containing 20% Polybutene produced no irritation, and repeated insult patch tests of 3.1–50% Polybutene in formulations produced, at most, minimal irritation in a small percentage of the test population. The products tested produced no irritation or sensitization. Photo patch tests of formulations with concentrations ranging from 15% to 50% Polybutene produced no reactions.

COMMENTS

Polybutenes are the isotactic polymers of isobutene and n-butene. Their stability in sunlight, low polarity, low degree of unsaturation, and closely packed, branched-chain molecular structure make them chemically inert. Polybutenes provide viscosity or emulsifiability to more than 80 cosmetic products in concentrations of 1% to >50%. They are primarily used in lipstick formultions, at concentrations greater than 10%. In addition, Polybutenes are widely used in lubricants, sealers, adhesives, fungicides, herbicides, and pesticides.

Commercial interest in Polybutenes extends beyond the cosmetic industry. The numbers and variety of animal toxicological studies conducted to establish their safety have been satisfactory. The results of acute oral toxicity tests of Polybutenes, alone and in formulations, show these materials to

be "relatively harmless."[81] When fed to rats at a concentration of 75%, the LD50 was greater than 34.6 g/kg, and a 30% lip lotion formulation had an LD50 greater than 40 g/kg for the formulation. Similarly, in percutaneous toxicity tests, rabbits showed no adverse systemic effects after exposure to Polybutenes.

In acute skin irritation tests, using several different formulations containing Polybutenes, rabbits showed no irritation or mild irritation. Other test results have also indicated that Polybutenes are not toxic: (a) there were no observable effects in rats after inhalation for 4 h in concentrations up to 18.5 mg/l of air; (b) there was only mild, transient eye irritation in rabbits treated with Polybutenes; (c) intravaginal application of concentrated Polybutene daily for 30 days produced no observable effect in rabbits; and (d) applications of Polybutene to the skin of rats produced no systemic effects.

Similar results were obtained in studies on chronic oral toxicity: rats fed up to 20,000 ppm Polybutene for 2 years and dogs fed up to 1,000 mg/kg daily for 2 years showed no disturbances attributable to the ingredient. Rats fed up to 20,000 ppm for three successive generations showed no impairment in reproduction. Ten percent Polybutene fed to rats for 6 months had no effects on their reproduction. It is evident from these animal tests that Polybutenes consistently have very low toxicity even at high doses and concentrations.

The available human clinical data, like the animal data, show very mild effects. Skin tests for sensitization, irritancy, phototoxicity, and photosensitization, however, used cosmetic formulations, and neither the pure ingredients nor the highest concentrations used in cosmetic products were evaluated. Nevertheless, the large numbers of patients used in these tests fulfill some of the requirements of these tests. Thus, notwithstanding the incompleteness of the human clinical tests, the animal toxicological studies have been sufficient to compensate for the deficiency, and their uniformly negative results permit the conclusion that Polybutenes are safe cosmetic ingredients.

CONCLUSION

On the basis of the available information, the Panel concludes that Polybutenes are safe as presently used in cosmetics.

ACKNOWLEDGMENT

Ms. Anne F. Moore, Scientific Analyst and writer prepared the literature review and technical analysis used by the Expert Panel in developing this report.

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