FINAL REPORT OF THE SAFETY ASSESSMENT FOR WHEAT GERM OIL

Wheat Germ Oil is used in a wide variety of cosmetic formulations at concentrations ranging from less than 0.1 to 50%.

The results of tests on laboratory animals and humans for the safety of Wheat Germ Oil and the numerous cosmetic products containing this material confirm the safety of Wheat Germ Oil as presently used in such products.

CHEMICAL AND PHYSICAL PROPERTIES

Composition

Wheat Germ Oil is obtained from wheat germ by hydraulic expression or solvent extraction. The germ yields about 7.2% of a light yellow or reddish-yellow oil (Drummond *et al.*, 1935a,b).

The major components of this oil are glycerides of linoleic, palmitic, and oleic acids, and it contains significant amounts of Vitamin E which vary appreciably in different samples of wheat. Since Wheat Germ Oil is obtained from natural sources, it is not surprising to find great variability in the composition of the oil obtained from different varieties of wheat grown under variable climatic conditions. Ranges of values for individual substances present in batches of Wheat Germ Oil are listed below (CTFA, 1978[1]; Windholz, ed., 1976).

	Percent
Glycerides of Saturated Fatty Acids	13. - 22.
Palmitic Acid	11. - 16.
Stearic Acid	1. - 06.
C20-22 Saturated Acids	0.0 - 01.2
Glycerides of Unsaturated Acids	
Oleic Acid	8. - 30.
Linoleic Acid	44. - 65.
Linolenic Acid	4. - 10.

[1]Available upon request. Administrator, Cosmetic Ingredient Review, Suite 212, 1133 15th St., NW, Washington, DC 20005.

Free Fatty Acids	3. - 5.
Unsaponifiables	2. - 6.
Lecithin	0.9 - 3.
Sterols	0.9 - 3.
Vitamin E Active Tocopherols	0.2 - 0.5 (minimum 2 I.U./g)

Properties

Wheat Germ Oil is a bland, yellow or reddish-yellow substance resembling corn oil. It is soluble in chloroform, ether, and benzene, slightly soluble in ethyl alcohol, and insoluble in water (CTFA, 1978[1]; Windholz, ed., 1976).

Ranges of values for some chemical and physical characteristics of Wheat Germ Oil are listed below (Drummond *et al.*, 1935a; CFTA, 1978[1]; Windholz, ed., 1976).

	Range
Refractive index	1.469 - 1.478
Specific gravity at 25/25°C	0.910 - .930
Acid value	6 - 20.
Saponification value	179 - 190.
Iodine value	115 - 134.
Iodine value of unsaponifiable fraction	97.6

(Drummond *et al.*, 1935)

Analytical Methods

The analytical methods developed for determining the individual component content of Wheat Germ Oil include column, thin layer, and gas-liquid chromatography (Fedeli, 1968; Gunstone and Hilditch, 1946; Karrer and Fadda, 1971; Koch and Pousold, 1953; Sheppard and Stutsman, 1977; Slover, 1967).

Impurities

No components of Wheat Germ Oil other than those listed have been reported. Solvent extraction may leave residual hexane, ethylene dichloride or other extraction solvent in unspecified amounts.

USE

Cosmetic Use

Wheat Germ Oil, mostly in concentrations of 0.1% but as high as 50% in one moisturizing preparation, is reported to be used in 113 cosmetic formulations representing a wide variety of products. Specific product types, associatated concentrations, and the number of product formulations for each concentration range are presented in Table 1 (FDA, 1976).

TABLE 1. Product Formulation Data (FDA, 1976)

Ingredient	Cosmetic Product Type	Concentration (%)	Number of Product Formulations
Wheat Germ Oil	Bath oils, tablets, and salts	>1 to 5	1
		>0.1 to 1	1
	Bubble baths	≤0.1	1
	Eye lotion	>0.1 to 1	1
		≤0.1	1
	Eye makeup remover	≤0.1	1
	Mascara	≤0.1	1
	Hair conditioners	>1 to 5	3
		>0.1 to 1	1
		≤0.1	3
	Hair sprays (aerosol fixative)	≤0.1	1
	Permanent waves	≤0.1	3
	Shampoos (noncoloring)	>0.1 to 1	1
		≤0.1	7
	Wave sets	≤0.1	4
	Hair shampoos (coloring)	≤0.1	1
	Foundations	>0.1 to 1	1
	Lipstick	>1 to 5	4
		>0.1 to 1	15
		≤0.1	2
	Makeup bases	>0.1 to 1	1
	Rouges	>0.1 to 1	5
		≤0.1	1
	Hair creams and lotions	>10 to 15	1
	Nail polish and enamel removers	>1 to 5	1
	Shaving cream (aerosol, brushless, lather)	≤0.1	1
	Other shaving preparations	>1 to 5	1
	Cleansing (cold creams, cleansing lotions, liquids, pads)	>1 to 5	5
		>0.1 to 1	2
		≤0.1	1
	Face, body and hands (excluding shaving preparations)	>1 to 5	2
		>0.1 to 1	3
	Moisturizing	>25 to 50	1
		>10 to 25	1
		>1 to 5	5
		0.1 to 1	7
		≤0.1	3
	Night	>1 to 5	1
		>0.1 to 1	2
		≤0.1	2
	Paste masks (mud packs)	>1 to 5	1
	Skin fresheners	>1 to 5	1

TABLE 1(continued). Product Formulation Data (FDA, 1976)

Ingredient	Cosmetic Product Type	Concentration (%)	Number of Product Formulations
	Other skin care preparations	>10 to 25	1
		>5 to 10	1
		>0.1 to 1	3
		≤0.1	2
	Suntan gels, creams, and lotions	>1 to 5	2
		>0.1 to 1	2
	Other suntan preparations	>0.1 to 1	1

The principal function which this material seems to fulfill derives from the antioxidant properties of the Vitamin E (alpha tocopherol) fraction. That is, its function appears mainly to be that of a preservative against oxidation and rancidity. Unspecified "aesthetic and application virtues" are also claimed (Calogero, 1978) and are very likely the decisive factors in the use of Wheat Germ Oil at high concentrations in cosmetic preparations. Discussions on the use of Wheat Germ Oil in cosmetics have been published in a number of articles (Hutterer, 1970; Neumann, 1951, 1966; Sherr-Bruzer, 1972; Sisley, 1955).

Non-Cosmetic Use

Wheat Germ Oil is used as a diet supplement because of its high Vitamin E content. Its use as a stabilizer to prevent oxidation in fatty materials and dairy products has been described (Berndt and Schilling, 1966; Chapman and McFarlane, 1946; Gershentsvit and Akkerman, 1960; Munin, 1942). The unsaplonifiable fraction of Wheat Germ Oil inhibits oxidative polymerization of frying oils (Sims *et al.*, 1972).

Pursuant to the Food and Drug Administration, Wheat Germ Oil is listed as a Generally Recognized as Safe (GRAS) food ingredient (21 CFR 170.30(d)).

BIOLOGICAL PROPERTIES

General Effects

The antioxidant action of Wheat Germ Oil exceeds that of the alpha-tocopherol component alone (Anzaldi, 1948).

Vitamin E is concentrated in the unsaponifiable fraction of Wheat Germ Oil. It is an essential factor in the human diet.

Secondary Effects

Endocrinology Evans and Bishop (1923) were among the first to recognize that Wheat Germ Oil contains a factor essential for reproduction. Female rats maintained on a Vitamin E deficient diet usually exhibited normal estrus,

ovulation, fertilization, and implantation, but abortion of the embryo invariably followed. Wheat Germ Oil in the diet cured this defect, and the authors assumed that the active factor was as undiscovered vitamin.

Vitamin E was subsequently isolated and identified as the reproductive factor present in the unsaponifiable fraction of Wheat Germ Oil (Evans and Bishop, 1924; Evans and Burr, 1924; Sure, 1924). In the presence of Vitamin E deficiency, implantation is unsuccessful in female rats, and male rats suffer progressive degeneration of the testes (Evans and Burr, 1925; Mattill *et al.*, 1924). on the other hand, overdoses of Vitamin E result in testicular atrophy in male hamsters and irreversible sterility in female rats (DiPalma and Ritchie, 1977). Other vegetable oils have similar but less potent effects on fertility (Sure, 1927).

Several studies on the reproductive effects of Wheat Germ Oil beyond the effects of Vitamin E have been conducted using farm animals, chiefly sheep and cattle, with both positive (Bay and Vogt-Moller, 1934; Dukelow, 1966a; Marion, 1962; Pacini, 1938; Tutt, 1933; Vogt-Moller and Bay, 1931) and negative (Dukelow, 1966a; Card, 1929; Dukelow, 1966b, 1965, 1963; Lentz, 1938; Salisbury, 1944; Titus and Burrows, 1940) results. A comprehensive review of this literature was published by Dukelow (1967). Cromer (1938) and Watson and Tew (1936) found that large amounts of Wheat Germ Oil administered before conception and continued throughout pregnancy prevented recurrent or threatened abortion in human beings.

The endocrinologic properties of Wheat Germ Oil were first demonstrated by Levin *et al.*, 1950). They reported that, in controlled experiments, Wheat Germ Oil produced by solvent extraction with ethylene dichloride favorably influenced conception, litter size, birth weights, and weaning weights of rats. A sufficient amount of the tocopherols was incorporated in the diets of both control and experimental groups to demonstrate that a substance other than Vitamin E was responsible for the estrogenic properties of Wheat Germ Oil. Levin, Burns, and Collins (1951) later found apparent estrogenic effects by injection and by oral adminstration of the oil to rats. The oil (a) elicited vaginal introitus in immature rats, (b) increased uterine weights in hypophysectomized animals, and (c) brought about estrus in ovariectomized animals. The authors also demonstrated "androgenic" activity with the chicken comb growth and rat seminal vesicle response methods. They further reported "gonadotropic" activity in rats and rabbits.

Many plants contain variable amounts of substances that, when injected subcutaneously into mice and rats, show estrogenic activity. Bradbury and White (1954) reviewed published reports on 55 plants that had been shown to have estrogenic properties and found that wheat seeds, flour, and germ oil have only detectable activity, no more than cherries, plums, or apples. These nearly ubiquitous plant substances contain diverse chemicals types gathered under the name of phytoestrogens. Phytoestrogens, the isoflavanoid compound coumestrol in particular, are weak estrogens whose biological effect in stimulating uterine hypertrophy in immature rats is approximately 2,800 times *less* effective than that of diethylstibestrol and about 200 times less effective than that of estrone (Bickoll *et al.*, 1962). Thus, it is likely that Wheat Germ Oil contains a

phytoestrogen, the potency of which is negligible in regard to estrogenic activity with cosmetic use.

As for gonadotropic and/or androgenic properties of Wheat Germ Oil, these effects, as well as the improved physical performance demonstrated by Cureton (1954, 1972) in human subjects who ingested Wheat Germ Oil, can now be explained by the fact that the oil contains octacosanol, a 28 carbon, straight-chain saturated alcohol (Levin *et al.*, 1962). Octacosanol, present in the unsaponifiable fraction at unspecified concentration, conforms to the structural formula CH_3 (CH_2) $_{26}CH_2OH$ and has a molecular weight of 410.74 (Windholz, ed., 1976). This substance exerts a profound effect on the metabolic processes; all the beneficial effects reported may be directly related to octacosanol, isolated or contained in its natural source, Wheat Germ Oil (Cureton, 1972; Wolf *et al.*, 1972). Levin (1963) using the method of Dorfman and Dorfman, applied octacosanol to the combs of White Leghorn chicks. Whereas there was highly significant increase in comb growth, the response was not dose-related; similar results were obtained with 1296 μg as with 0.00036 μg. Such all-or-none responses were in striking contrast with the graded dose reponse to testosterone. The stimulation of chicken comb growth with octacosanol, then, is "not a true androgenic effect" (Levin, 1963). Thus, the available evidence of potential dangers from exposure to endocrinologically active agents in Wheat Germ Oil must be considered negligible, particularly in the context of current considerations.

Neurophysiology Wheat Germ Oil has been tested in the therapy of muscular dystrophy and other neurologic disorders with positive results in mammals (Goettsch and Ritzmann, 1939; King *et al.*, 1955; March, 1946; Morgulis and Spencer, 1936) and negative results in fowl (Johnson, 1940; Jungherr, 1940; Norris, 1940).

Wheat Germ Oil has also been employed in humans. Positive results were obtained when Stone (1949) administered the oil over a ten-year period to children who had a variety of neuromuscular disturbances and other disturbances of the nervous system. Rabinovitch *et al.* (1951) found similar results with Wheat Germ Oil therapy over periods ranging from months to 12 years in 107 cases of neuromuscular disorder.

Other physiological effects Schwarz (1944a,b) reported that Wheat Germ Oil protected the liver of rodents from injury induced by a deficient Casein-VI diet.

Vitamin E protects against ozone inhalation damage in rats (Dillard *et al.*, 1978; Dumelin *et al.*, 1978).

Alpha-tocopherol reacts with sodium nitrite in an acidic gastric fluid environment with the resulting disappearance ot the nitrite anion from the reaction mixture. Thus, it inhibits the formation of nitrosamines from nitrosatable amines and nitrite in the stomach (Kamm *et al.*, 1977).

Vitamin E, Wheat Germ Oil, and its aqueous extract were found to diminish permeability to glucose in the red blood cells of normal persons (Orskov, 1943).

Blood samples from 17 healthy girls who ingested 60 g of Wheat Germ Oil

per day showed a 16% decrease in serum cholesterol levels (Suzuki *et al.*, 1965). This effect was attributed to the linoleic acid and unsaponifiable contents of the oil.

Vitamin E appears to promote the healing of burns, trauma-induced wounds, and ulcers (Hellstrom, 1961). Vitamin E also raises the skin temperature (Kunzmann, 1961).

Absorption, Metabolism, Storage, and Excretion

The rate of skin absorption of Wheat Germ Oil has been measured in rats and compared to that of other oils. The absorption was fastest for linseed oil and slowest for rice oil, with Wheat Germ Oil having an intermediate rate of absorption (Valette and Sobrin, 1963).

Animal Toxicology

Acute Studies - Oral Toxicity A single dose of 5 g/kg Wheat Germ Oil was given by gavage to each of five male and five female rats (CTFA, 1978b). There were no deaths, no observed symptoms, and no gross pathological changes at autopsy 14 days after treatment. Although there was no control group for comparison, weight gain appeared normal.

Acute Studies - Eye Irritation Six out of 10 rabbits tested by the Draize method showed transient mild irritation of the conjuntiva or iris when two drops of undiluted Wheat Germ Oil were placed in the eye (CTFA, 1959a). The highest average score of the group was 1.1 out of a possible maximum total of 110. All scores were zero after the third day.

Similar findings were obtained in tests on 2 groups of 6 rabbits each. Eyes were treated with 0.1 ml samples of 100% Wheat Germ Oil and 2% Wheat Germ Oil in a water emulsion, respectively (CTFA, 1978c). The highest average score for the group receiving the 100% Wheat Germ Oil was 0.3 after 2 days. This score fell to zero after three days. The score of the other group was zero throughout.

Numerous finished cosmetic products containing Wheat Germ Oil in various concentrations were tested in rabbits (CTFA, 1977). These included shampoos, conditioners, hair sprays, spray conditioner and lusterizer, body waves, styling gel, and hand and body lotions. As expected, eye irritation was seen in several cases, but none of these reactions could be attributed to Wheat Germ Oil.

Acute Studies - Skin Irritation Wheat Germ Oil at 100% and at 2% in a water emulsion showed skin irritation scores of 0.15 and 0, respectively, in a standard Draize test on intact and abraded skin of rabbits (CTFA, 1978d). Similar tests on shampoos, hair sprays, conditioners, and hand and body lotions containing Wheat Germ Oil resulted in mild irritations, with scores ranging from 0 to 5.75 (CTFA, 1977).

Miscellaneous Acute Toxicity Studies

1. A guinea pig sensitization test with 100% Wheat Germ Oil (CTFA, 1978e) showed no evidence of allergic properties for this material.

2. Wheat Germ Oil was tested for irritation of the penis and scrotal sac in 6 rabbits to which 1 ml of the undiluted oil was applied daily for 5 days (CTFA, 1978f). Only 1 of the 6 animals showed a slight redness on the second and fourth days. All were completely negative on day 5.
3. The acute inhalation toxicity of a spray conditioner and lusterizer containing ≤0.1% Wheat Germ Oil was tested in rats exposed to 200 mg/liter of air for 1 hour. The computed average inhaled dosage was 32.2 mg of the formulation per kg of body weight. No physical or behavioral effects were noted in the following 14 days (CTFA, 1977).

Subchronic Studies A subchronic (12-week) feeding study on 5 male and 5 female weanling rats fed a diet containing 25% Wheat Germ Oil failed to show any evidence of adverse effects of the material under investigation (CTFA, 1959b). The death of one female at 10 weeks was not attributed to effects of the test material.

Chronic Studies Rowntree *et al.* (1937a) first reported the development of malignant, transplantable tumors in rats fed a diet that contained crude ether-extracted Wheat Germ Oil. Later he (Rowntree *et al.*, 1937b,c; Rowntree and Ziegler, 1943) and his collaborators (Dorrance and Ciccone, 1937) reported similar experiments with similar results. Rowntree and Ziegler(1943), however, reported a subsequent inability to produce tumors by feeding Wheat Germ Oil to rats. All other available reports indicated that Wheat Germ Oil expressed or extracted in a variety of different ways is not tumorigenic (Auchincloss and Haagensen, 1939; Blumberg, 1940; Brues *et al.*, 1941; Bryan and Mason, 1940; Carruthers, 1939; Day *et al.*, 1939; Demole, 1939; Dingemanse and Van Eck, 1939; Dittmar and Burschkies, 1939; Evans and Emerson, 1939; Ginzton and Connor, 1940; Haddow and Russell, 1937; Halter, 1939; Harris, 1947; Rider, 1940). A careful analysis of the available data suggests that Wheat Germ Oil does not contain a carcinogenic agent.

Clinical Assessment of Safety

Clinical Oral Ingestion Wheat Germ Oil has long been used as a nutritive supplement high in Vitamin E and unsaturated fatty acids. No adverse reactions resulting from such use have been brought to our attention.

In a recent study, 28 adults ingested 100 to 800 international units of Vitamin E daily for three years. Plasma alpha-tocopherol was elevated to an average of more than twice the 650 μg/100 ml. level in controls. No apparent toxicity was observed (Farrell and Bieri, 1975).

Dermatologic Evaluation The available data suggests that Wheat Germ Oil is not a potent irritant or contact sensitizer.

In one study, Schwartz-Peck 48-hour patch tests were performed on 100 subjects with concentrations of 1, 10, and 50% Wheat Germ Oil in mineral oil. No positive reactions were noted. Draize and/or maximization methods, however, were not used in this study (CTFA, 1978g).

Two petrolatum-based hair dressings containing Wheat Germ Oil (1 and 1.1%) were tested for contact sensitization using a Draize repeated insult patch

test procedure on 53 predominantly black male and female subjects. The products were found to be "essentially nonirritating" and nonsensitizing. One subject appeared to have been sensitized to a component of the 1% sample; the sensitizer was not identified. A similar procedure was used to test an oil and water emulsion hand cream containing 1% Wheat Germ Oil on 51 black male and female subjects. This material was also found to be "essentially nonirritating" and nonsensitizing. Blacks are generally considered to be less sensitive to primary irritants, and this factor may have biased the results of these studies (Hill Top Research, 1976a, b).

Industry estimates over 500,000,000 unit packages of cosmetics containing Wheat Germ Oil and related materials have been marketed with no known adverse effect (Calogero, 1978). The reliability of this form of reporting is difficult to evaluate.

SUMMARY

Wheat Germ Oil is used in a wide variety of cosmetic formulations at concentrations ranging from less than 0.1 to 50%. It is applied to all skin areas and has the opportunity for absorption by several routes.

There are data supporting the conclusion that Wheat Germ Oil in low concentrations (1%) in specific product formulations is nonsensitizing and nonirritating to the human skin. Forty-eight-hour patch tests with up to 50% Wheat Germ Oil produced no evidence of irritation. Data from provocative or maximization testing of this material in a wide range of concentrations are, however, lacking.

Tests for eye and skin irritation in rabbits have shown only occasional minimal and rapidly reversible effects. No evidence of sensitization was observed in tests with the oil.

Acute and subchronic feeding studies on rats fed high levels of wheat Germ Oil provided results which indicate no risk from accidental oral ingestion of the oil as contained in cosmetic products. These studies illustrate the wide range of safety and lack of significant systemic toxicity of ingested Wheat Germ Oil.

The finding of malignant abdominal tumors in rats fed ether-extracted crude Wheat Germ Oil in repeated tests by one group of workers and the later failure of that same group and of numerous other groups of investigators to duplicate such a finding have never been explained. In spite of early reports, all investigators agree that Wheat Germ Oil is not carcinogenic when administered orally to the rat.

The results of several studies have suggested that What Germ Oil may possess estrogenic, androgenic, and gonadotropic activities and have favorable effects on reproduction in several animal species fed this material. A careful review of all evidence, however, demonstrates that Wheat Germ Oil possesses no true androgenic or gonadotropic acitivity and only insignificant estrogenic activity.

The results of tests on laboratory animals and humans for the safety of Wheat Germ Oil and the numerous cosmetic products containing this material confirm the safety of Wheat Germ Oil as presently used in such products.

CONCLUSIONS

On the basis of the available information presented herein, the Panel concludes that Wheat Germ Oil is safe as a cosmetic ingredient in the present practices of use and concentration.

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[1]Available upon request. Administrator, Cosmetic Ingredient Review, Suite 212, 1133 15th St., NW, Washington, DC 20005

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