Final Safety Assessment

Decyl Glucoside and Other Alkyl Glucosides as Used in Cosmetics

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ABSTRACT

The CIR Expert Panel assessed the safety of 19 alkyl glucosides as used in cosmetics. Most of these ingredients function as surfactants in cosmetics, but some have additional functions as skin conditioning agents, hair conditioning agents, or emulsion stabilizers. The Panel reviewed the available animal and clinical data on these ingredients. Since glucoside hydrolases in human skin are likely to break down these ingredients to release their respective fatty acids and glucose, the Panel also reviewed CIR reports on the safety of fatty alcohols, and were able to extrapolate data from those previous reports to support safety. The Panel concluded that these alkyl glucosides are safe in the present practices of use and concentration when formulated to be non-irritating.

INTRODUCTION

This assessment reviews data relevant to the safety of decyl glucoside and 18 other alkyl glucoside ingredients as used in cosmetic formulations. Most of these ingredients function in cosmetics as surfactants. Other reported functions of some of these ingredients are skin conditioning agent, hair conditioning agent, or emulsion stabilizer. Hexadecyl D-glucoside and octadecyl D-glucoside are not listed in the *International Cosmetic Ingredient Dictionary and Handbook*, but are being included because they are listed by the Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) as being used in cosmetic formulations.

The ingredients included in this review are obtained by the condensation of an alcohol with a cyclic form of glucose (D-glucopyranose). The group includes:

Decyl Glucoside
Arachidyl Glucoside
Butyl Glucoside
C10-16 Alkyl Glucoside
C12-18 Alkyl Glucoside
C12-20 Alkyl Glucoside
C20-22 Alkyl Glucoside
Caprylyl/Capryl Glucoside
Caprylyl Glucoside
Cetearyl Glucoside
Coco-Glucoside
Ethyl Glucoside
Hexadecyl D-Glucoside
Isostearyl Glucoside
Lauryl Glucoside
Myristyl Glucoside
Octadecyl D-Glucoside
Octyldodecyl Glucoside
Undecyl Glucoside

Although the names of these ingredients imply that they are mono-glucosides, these ingredients are not limited to mono-glucosides, but may involve products that are the result of a number of condensed glucose repeat units.

Glucoside hydrolases in human skin are likely to break down these chemicals to release their respective fatty alcohols and glucose. Therefore, summary information on the appropriate fatty alcohols that have previously been reviewed by the Cosmetic Ingredient Review (CIR) is presented at the end of this report in the last table (Table 6).

CHEMISTRY

Definition and Structure

This group of ingredients consists of anomerically-alkyl-substituted D-glycopyranosides. Specifically, the alkyl substituents range from 2 to 22 carbons in length, and the D-glycopyranosides consist of glucose-type mono-, di-, tri-, oligo-, or poly-saccharides (e.g., mono = glucose (i.e. D-glucopyranoside) and di = maltose (i.e. D-maltopyranoside)). The degree of polymerization of these ingredients refers to the number of glucose monomers (n in Figure 1). For example, a degree of polymerization of 2 means the di-glucose (disaccharide), maltose. Regardless of the degree of polymerization these ingredients are simply named "glucosides." Although these ingredients are most likely the ß-anomers, the names of these alkyl glucosides are not necessarily specific to either anomer.

The general decyl glucoside structure shown in Figure 1 is the ten-carbon, alkyl-chain substituted glycopyranoside, wherein n can be 1 (for a mono-glucoside) or more (for di-, tri-, oligo-, and poly-glucosides):

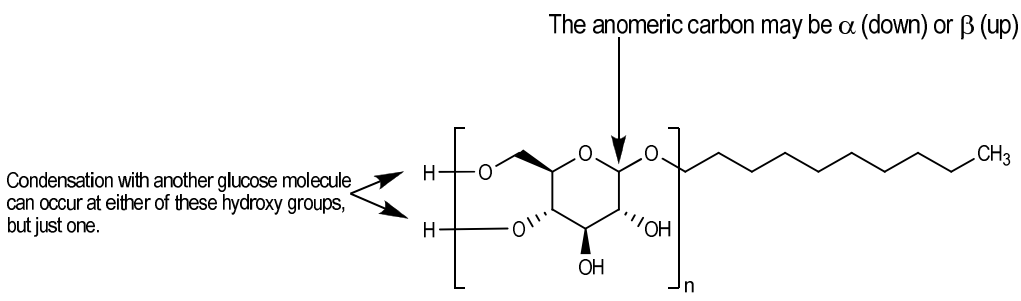


Figure 1. General Decyl Glucoside Structure

Therefore, decyl glucoside may be monomeric or polymeric, but the International Nomenclature Cosmetic Ingredient (INCI) name will still be decyl glucoside. "Poly" will be used generically used throughout the rest of this report to refer to di-, tri-, oligo-, poly-glucosides, and mixtures thereof. Decyl glucoside, for example, may consist of one or more of the following polyglucosides (in this case isomaltopyranosides) shown in Figure 2:

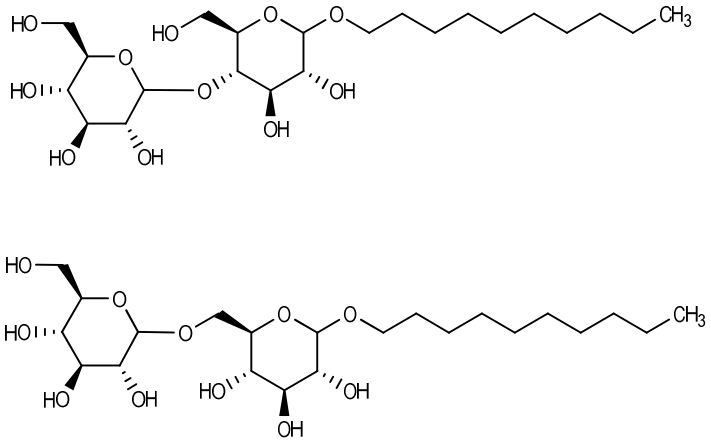


Figure 2. Examples of Decyl Glucoside Forms

A decyl glucoside with a degree of polymerization of 1.6, for example, would then be a mixture comprised of decyl glucopyranoside and one of the decyl maltopyranosides (with a slightly higher percentage of the maltose derivative) shown in Figure 2. Because many of these fatty alcohols are supplied from natural feed stocks, the designated length may be the average (e.g., median) length (e.g. decyl glucoside may actually be a mixture of C6, C8, C10, C12, C14, and C16 chain lengths, each anomerically attached to a glucopyranose).[1]

The definitions and structures of the ingredients included in this review are provided in Table 1.

Impurities, Constituents, and Physical and Chemical Properties

These compounds are typically solids, with solubility in both aqueous and organic solutions. The available impurity, constituent, and physical and chemical property information is presented in Table 2.

Method of Manufacture

The first report of the synthesis of alkyl glucosides in 1893 involved reacting glucose with anhydrous ethanol under acidic conditions to produce ethyl glucoside.[2] Alcoholysis of glucose and polysaccharides under acidic conditions is still the method of choice. It is considered to be a "green" process that can involve the use of natural and renewable sources (e.g., the alcohols can be obtained from coconut oil or palm oil and the glucose or polysaccharide can be obtained from corn, potato, or wheat starch).[3] Of note, the reaction conditions that produce an ether linkage between a fatty alcohol and the anomeric hydroxy group of glucose are known to cause condensation of one molecule of glucose with another molecule of glucose, thereby producing alkyl *poly*glucosides (APGs) even when an alkyl *mono*glucoside may be the intended product.

USE

Cosmetic

The alkyl glucosides named in this safety assessment are reported to function primarily as surfactants.[4] A few are reported to function as skin conditioning agents, hair conditioning agents, or emulsion stabilizers.

VCRP data obtained in 2011 for this ingredient group indicate that decyl glucoside has the highest frequency of uses reported, 492; the majority of these uses, 421, are in rinse-off formulations.[5] Cetearyl glucoside, lauryl glucoside, and coco-glucoside have 477, 399, and 350 reported uses, respectively. Cetearyl glucoside is reported mostly to be used in leave-on products. The remaining ingredients that are reported to be used have ≤75 uses. Based on data from a survey conducted by the Personal Care Products Council (Council), lauryl glucoside has the highest leave-on concentration of use at 8%; this leave-on use is in a hair color spray; it also is reported to have the highest leave-on concentration of use that involves dermal contact, and that concentration is 5%. Decyl glucoside has the highest rinse-off concentration of use, at 33%.[6] Two ingredients, hexadecyl D-glucoside and octadecyl D-glucoside are not listed in the *International Cosmetic Ingredient Dictionary and Handbook*, but are listed by the FDA VCRP as being used in cosmetic formulations; hexadecyl D-glucoside was also had use concentration data reported by industry.

Frequency and concentration of use data are provided in Table 3a. In some cases, reports of uses were received in the VCRP, but no concentration of use is available. For example, decyl glucoside is reported to be used in 25 baby products, but no use concentration was available. In other cases, no reported uses were received in the VCRP, but a use concentration

was provided in the industry survey. For example, caprylyl glucoside was not reported in the VCRP to be used in non-coloring hair products, but the industry survey indicated that it was used in such products at 4%. It should be presumed that caprylyl glucoside is used in at least one hair care product. The ingredients not listed in the VCRP or by the Council as in use are listed in Table 3b.

Products containing alkyl glucosides are reported to be used on baby skin or applied to the eye area, and mucous membranes may be exposed to these products. Coco-glucoside is reported to be used in a product that could be ingested. Some of the alkyl glucosides are used in cosmetic sprays, including hair and body and hand sprays, and could possibly be inhaled. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters >10 µm, with propellant sprays yielding a greater fraction of droplets/particles <10 µm compared with pump sprays.[7,8] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (i.e., able to enter the lungs) to any appreciable amount.[9,10] However, the potential for inhalation toxicity is not limited to respirable droplets/particles deposited in the lungs. Inhaled droplets/particles deposited in the nasopharyngeal and thoracic regions may cause toxic effects depending on their chemical and other properties. There is some evidence indicating that deodorant spray products can release substantially larger fractions of particulates having aerodynamic equivalent diameters in the range considered to be respirable.[10] However, the information is not sufficient to determine whether significantly greater lung exposures result from the use of deodorant sprays, compared to other cosmetic sprays.

All of the glucosides named in the report, with the exception of C20-22 alkyl glucoside, hexadecyl D-glucoside, and octadecyl D-glucoside, are listed in the European Union inventory of cosmetic ingredients.[11]

Non-Cosmetic

Caprylyl glucoside and similar alkyl glucosides are effective solubilizers of lipids and proteins below their critical micelle concentrations (CMC), and are used in various biochemical techniques and membrane research. These ingredients also can be used to reconstitute enzymes or other proteins from crude biological preparations.[12]

The use of decyl glucoside as a stabilizer in nanosuspensions for dermal delivery has been investigated; decyl glucoside was effective as a stabilizer with resveratrol[13] and hesperetin ((S)-2,3-dihydro-5,7-dihydroxy-2-(3-hydroxy-4-methoxy-phenyl)-4H-1-benzopyran-4-one)[14] nanosuspensions.

TOXICOKINETICS

Absorption, Distribution, Metabolism, and Excretion

Dermal

Glucoside hydrolases are known to be present in human skin. Therefore, the first step in the metabolism of these ingredients may be breaking down these chemicals to glucose and their respective fatty alcohols.[15]

In Vitro

Caprylyl/Capryl Glucoside

The dermal penetration of caprylyl/capryl glucoside, diluted to 10% in Hanks' buffered salt solution, pH 6.5, was evaluated *in vitro* using human skin.[16] Two skin samples from each of three donors were used in the study (n=6). The receptor fluid was Krebs ringer's bicarbonate buffer without HEPES and glucose. After 24 h, the mean recovery was 0.52% of caprylyl/capryl glucoside from two tape strips and 0.30% of caprylyl/capryl glucoside in the further 18 tape strips. The mean amount of caprylyl/capryl glucoside removed from the skin (by washing) ranged from 109-145% of the dose applied. The mean absorbed dose of caprylyl/capryl glucoside, as the sum of the amounts found in the viable epidermis, dermis, and receptor medium, was 0.01%.

Oral

Non-Human

Caprylyl Glucoside

Three female NMRI mice were given a single oral dose, by gavage, of 37 MBq/mmol caprylyl [U-^{14}C]glucoside in 0.05 ml of a 5% aq. solution of phophatidylcholine.[17] The animals were killed 2 h after dosing. The highest levels of radioactivity were found in the stomach, intestines, liver, and kidneys, with most of the radioactivity (81-98%) distributed in the aqueous phase. High levels of radioactivity that were not extractable with chloroform were found in the urine, which, according to the researchers, indicated a high rate of degradation to water-soluble metabolites.

In the stomach, 75% of the radioactivity was associated with unchanged substrate. In the kidneys and intestines, 50% of the total radioactivity was unchanged substrate, while only a trace amount found in the liver was associated with unchanged substrate. Labeled glucose was detected in all four of these organs. In the stomach, intestines, and kidneys, 13-19% of the radioactivity was contained in the chloroform extract, and most of it was derived from caprylyl [U-^{14}C]glucoside. In this extract in the stomach, approximately 2% acylated-labeled substrate was detected.

Ethyl Glucoside

Groups of 6 male Wistar ST rats were fed a diet for 39 days in which sucrose was replaced with 10 or 20% ethyl glucoside, and a control group was fed unaltered (i.e., sucrose-containing) feed.[18] A 24-h urine collection was made once

weekly to check volume. Approximately 60-90% of the ethyl glucoside ingested by treated animals was recovered in the urine.

Absorption Enhancement

Caprylyl glucoside has been shown to increase the absorption of poorly absorbed drugs (e.g., insulin) both in vitro across human carcinoma monolayers and in vivo through mucosal membranes. In the in vitro study, the enhancement of the permeability of insulin across T84 and Caco-2 cell monolayers by caprylyl glucoside was concentration-dependent; permeability of insulin was not significantly enhanced at concentrations of 0.2 and 0.3%, while it was enhanced with 0.4 and 0.5% caprylyl glucoside.[19]

In a transmucosal absorption study, the effect of caprylyl glucoside on the nasal, buccal, and rectal absorption of insulin was examined using male Lewis rats.[12] A 5% solution of caprylyl glucoside had an enhancing effect on buccal absorption. The effect of other alkyl glycosides, including decyl and lauryl glucoside, on mucosal penetration was also evaluated. A 5% solution of decyl glucoside also enhanced the buccal absorption of insulin, but 5% lauryl glucoside did not have a significant effect. The researchers stated that there was no consistent relationship between alkyl chain length and penetration enhancement.

TOXICOLOGICAL STUDIES

Single Dose (Acute) Toxicity

Dermal

Caprylyl/Capryl Glucoside

Groups of 5 male and 5 female New Zealand White (NZW) rabbits were given a single dermal dose of 2 g/kg bw caprylyl/capryl glucoside, 50% active ingredient (a.i.) (as C8/C10 APG); the degree of polymerization, n, was 1.6.[20] (Whether occlusion was used was not stated.) Mild to moderate irritant effects, fecal staining, yellowing around the application site, emaciation, nasal discharge, and lacrimation were observed. One animal died of an unrelated infection, and at necropsy, 5 had spotty areas of hemorrhage on the lungs.

C10-16 Alkyl Glucoside

Groups of 5 male and 5 female NZW rabbits were given a single dermal dose of g/kg bw C10-16 alkyl glucoside, 50% a.i. (as C10-16 APG; n:1.6).[20] (Whether occlusion was used was not stated.) Slight depression, hunched posture, mild to marked erythema, and marked desquamation were observed. None of the animals died during the study.

Oral

Caprylyl Glucoside

Female NMRI mice were given a single oral dose of 0.040 g (2 g/kg bw) caprylyl glucoside as a suspension in 0.2 ml of a 5% aq. solution of phosphatidylcholine.[17] No toxic effects were observed during a 2-wk post-dose observation period. Growth and behavior were not affected.

Caprylyl/Capryl Glucoside

Groups of 5 male and 5 female Sprague-Dawley rats were given a single oral dose of 5 g/kg bw caprylyl/capryl glucoside (as C8/10 APG; n:1.6, 50% a.i.).[20] None of the animals died during the study.

C10-16 Alkyl Glucoside

Groups of 5 male and 5 female Sprague-Dawley rats were given a single oral dose of 5 g/kg bw C10-16 alkyl glucoside (as C10/16 APG; n:1.6, 50% a.i.).[20] None of the animals died during the study. Additionally, no mortality was observed upon dosing of 2 male and 2 female Wistar rats with a single oral dose of 2 g/kg bw C12/14 APG, n: 1.6 and 60% a.i.

Repeated Dose Toxicity

Dermal

Caprylyl/Capryl Glucoside

Groups of 6 male and 6 female NZW rabbits were dosed dermally with 0, 0.9, and 1.8 g a.i./kg (0, 22.5, and 45 w/v%, respectively) caprylyl/capryl glucoside (60% active) in distilled water (4 ml/kg).[21,22] Ten 6-h occlusive applications were made over a 2-wk period. Treatment-related signs of toxicity, such as ataxia, lethargy, and emaciation, were observed in both test groups. One female of the 1.8 g a.i./kg group died after 10 doses, and the death was considered test article-related. Slight irritation was observed 1 day after the initial dose, and severe dermal irritation was observed in males and females of both test groups by days 5-6 of the study. Body weights of treated male and female rabbits were significantly less than those of controls, and mean body weight loss was observed for both groups. Significant changes were observed in some hematology and clinical chemistry values; a dose-response relationship was not observed for most of the hematology changes. Compared to controls, absolute testes weights were significantly lower in treated males of both dose groups. No other compound-related changes in organ weights were observed. Small testes were observed in 3 of the 6 treated males of each group; the researchers stated that occurrence of this lesion was rare, and while the occurrence was not statistically significantly different from controls, it was considered biologically significant. Microscopic examination of selected male tissues reported very slight to marked testicular degeneration in all rabbits in the 0.9 g a.i./kg group and slight to marked testicular degeneration in four rabbits of the 1.8 g a.i./kg group. Very slight to moderate atrophy of the prostate and "accessory sex glands" was observed in 3 rabbits of each group. The researchers stated that irritation, inflammation, and stress in these animals were major contributing factors to many, if not all, of the toxicologic effects; however, the researchers also stated

that it is possible that caprylyl/capryl glucoside produced some of the effects. (Published findings have reported that degenerative changes occur commonly in the testes of normal rabbits, and these changes may be increased during stress.[23]) A NOEL was not obtained.

In another 2-wk study, 10 occlusive applications of 0.14, 0.41, and 1.25 g a.i./kg (60% active) caprylyl/capryl glucoside in distilled water (0, 3.5, 10.4, and 31.1% a.i., respectively) were made to intact skin on the backs of 6 male NZW rabbits per group in order to determine the NOEL for testicular toxicity.[24,25] Two of the high dose animals died during the study, and the 4 surviving animals had signs of treatment-related toxicity. No treatment-related mortality occurred in the low or mid-dose groups. Dermal irritation, which progressed from slight to severe with time, was observed in all test groups, and slight to moderate irritation was observed in the controls. Changes in some hematology and clinical chemistry values were observed, but were attributed to stress of the occlusive procedure, irritation, and body weight loss. A decrease in the mean absolute testicular weights in animals of the mid- and high dose groups was considered treatment-related. A treatment-related loss in body weight was observed in all test groups, and the mean terminal body weights of rabbits of all test groups were decreased compared to controls. Relatively small testes were observed in 1, 2, 4, and all 6 males of the control, low. mid and high dose groups, respectively. Treatment-related microscopic changes were observed in the testes, epididymides, prostate, and vesicular glands of the mid and high dose group animals; some of the lesions included an increased incidence and severity of diffuse bilateral testicular atrophy with necrotic spermatocytes and atrophy of the prostate and vesicular glands. The NOEL for the microscopic effects in the epididymides, prostate and vesicular gland was 0.14 g a.i./kg. One rabbit of the low dose group, which had the greatest body weight loss, had moderate testicular atrophy and a moderate amount of necrotic spermatocytes/spermatids. The researchers stated that the testes and accessory sex organs of the animals in the control and treatment groups were relatively immature due to age (12 wks) and low body weights, and the immature nature of these organs complicated the evaluation. Changes in the testes and accessory sex glands were attributed to the stress. An NOEL for the study was not established.

In another 2-wk study, using non-occlusive applications, 2 ml of 0, 0.06, 0.18, or 0.54 g a.i./kg caprylyl/capryl glucoside (60% active) in distilled water (corresponding to concentrations of 0, 3, 9, and 27% a.i., respectively) were applied to the intact skin of the backs of 6 male rabbits/group.[26] These doses were selected following a 2-wk pilot study, in which unoccluded exposure to 0.12, 0.23, and 0.45 a.i. g/kg caprylyl/capryl glucoside produced slight to moderate erythema and edema. In the main study, treatment-related signs of toxicity were not observed. Slight dermal irritation was observed in all groups after the initiation of dosing; the irritation became moderate in the high dose group after 3 days of dosing. Body weights of rabbits of the high dose group were slightly, but significantly, decreased compared to controls. Absolute testes weights were slightly, but not significantly, decreased in the high dose group. No treatment-related effects on hematology or clinical chemistry values or organ weights were reported. Microscopically, epithelial hyperplasia, hyperkeratosis, congestion, and eschar formation were observed in the skin of rabbits of the high dose group; these changes were not observed in rabbits of the other test groups. No test article-related microscopic changes were observed in the testes or accessory sex glands at any dose. The NOEL for systemic toxicity was 0.18 g a.i./kg caprylyl/capryl glucoside.

Oral

Ethyl Glucoside

In a study described earlier under "Toxicokinetics," in which groups of 6 male Wistar ST rats were fed for 39 days a diet in which sucrose was replaced with 10 or 20% ethyl glucoside, body weight gains, but not final body weights, were statistically significantly decreased in the 20% group when compared to control values.[18] All animals survived until study termination. Total water intake was increased with increased ethyl glucoside consumption. In animals fed ethyl glucoside, kidney weights were statistically significantly increased and epididymal and abdominal fatty pad weights were statistically significantly decreased. The renal tubules of 2 and 4 control rats were "not-dilated" and "slightly dilated," respectively, and the renal tubules of all the rats in 10% group were "slightly dilated." In the group fed 20% ethyl glucoside, the renal tubules of 3 rats were "slightly dilated", while the other 3 had "moderately-dilated" renal tubules. No microscopic damage to renal cells was observed.

Alkyl Polyglucosides (APG)

Groups of 10 male and 10 female Sprague-Dawley rats were dosed orally, by gavage, with 0, 0.25, 0.5 and 1 g/kg bw C12/16 APG for 13 wks.[20] An additional 5 male and 5 female control and high dose rats were used as a recovery group. No treatment-related changes in body weights, organ weights, or biochemistry or hematology parameters were observed. Absolute gonad weights were decreased in all test groups, but the decrease was not considered treatment related by the researchers because of a lack of a dose-response. A dose-dependent, slowly reversible, irritation and ulceration of the forestomach mucosa was observed in animals of the 0.5 and 1 g/kg bw groups. Systemic toxicity was not observed in any group. The no-observed adverse effect level (NOAEL) for systemic toxicity was 1 g/kg bw. The no-observed effect concentration for "local compatibility" was deduced as 2.5% a.i.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Dermal

Caprylyl/Capryl Glucoside

Repeated dose dermal toxicity studies with caprylyl/capryl glucoside (60% active), cited earlier, reported decreased testes weighs, small testes, testicular degeneration, atrophy of the prostate, and microscopic changes in the testes, epididymides, prostate, and vesicular glands. [21,22,24-26] These effects were observed in studies using occlusive wraps, but not in non-occlusive testing. These effects were attributed to the stress of the study, and possible irritation or inflammation.

Oral

Lauryl Glucoside

Groups of 24 gravid female Sprague-Dawley CD rats were dosed orally, by gavage, with 0, 0.1, 0.3, or 1 g/kg bw/day lauryl glucoside (as C10-14 or C10-16, n: 1.4) on days 6-15 of gestation.[27] All animals were killed on day 20 of gestation. No maternal toxicity was observed, and no reproductive or developmental effects were indicated. There were also no differences in external, visceral or skeletal malformations between groups. The NOAELs for maternal toxicity, embryotoxicity/fetotoxicity, and teratogenicity were all 1 g/kg bw/day.

Lauryl glucoside (as APG C12-C14 fatty alcohol from renewable sources, n: 1.43) was given orally, by gavage, to groups of 10 male and 10 female Sprague-Dawley rats at doses of 0, 0.1, 0.3, or 1 g/kg/day, from 2 wks prior to mating to 4 days after delivery.[27] No signs of general toxicity were observed in the parental animals. The relative and absolute weights of the testes, epididymides, and seminal vesicles were similar for treated and control animals. There were no test article-related effects on reproductive parameters. The mean litter weights, mean pup weights, sex ratio, and gestation period was similar for all groups; a slight variation in pre-birth loss observed in the high-dose group was not statistically significant. There were no treatment-related effects observed for the neonates.

In Vitro Estrogenicity Assays

Lauryl Glucoside

Lauryl glucoside (as APG C12-C14 fatty alcohol from renewable sources, n: 1.43) was evaluated in the E-Screen assay, in which the induction of cell proliferation in the estrogen-dependent human breast tumor MCF-7 cells is determined, at concentrations of 0.1-10,000 nmol/ml.[27] 17-β-Estradiol and bisphenol-A were reference substances, and the medium was the negative control. No effects were reported at concentrations up to 10^5 higher than the concurrent controls.

The effects of 0.1-1000 nmol/ml lauryl glucoside (as APG C12-C14 fatty alcohol from renewable sources, n: 1.43) were determined in the MCF-7 reporter gene assay, in which the induction of luciferase activity in stable transfected MCF-7 cells is determined.[27] No effects were seen with lauryl glucoside alone, and no anti-estrogenic or other synergistic effects were observed after incubation with 0.01-1000 nmol/ml estradiol:lauryl glucoside (1:1 molar ratio).

GENOTOXICITY

Alkyl Polyglucosides (APG)

The mutagenic potential of APGs (chain length not specified) was determined in two Ames tests at concentrations of 8-500 µg/l and 11-900 µg/plate, with and without metabolic activation.[20] APGs were not mutagenic. Positive and negative controls gave expected results.

The genotoxic potential of C10/16 APG was evaluated in an assay for chromosomal aberrations using Chinese hamster V79 lung fibroblasts, at concentrations of ≤160 µg/ml with and ≤16 µg//ml without metabolic activation.[20] C10-16 alkyl glucoside was not clastogenic in this assay. Positive and negative controls gave expected results.

CARCINOGENICITY

Published carcinogenicity studies were not found.

IRRITATION AND SENSITIZATION

Dermal Irritation and Sensitization

Dermal irritation and sensitization studies are summarized in Table 4. In dermal repeated dose (2-wk) toxicity tests using rabbits, caprylyl/capryl glucoside (60% a.i.) tested at concentrations ranging from-3.5-45% a.i. in distilled water produced severe irritation over time at all concentrations tested; in a non-occlusive study, slight dermal irritation was seen in similar testing with 3 and 9% (a.i.) caprylyl/capryl glucoside, and moderate irritation was reported with 27% a.i. after 3 days of testing. Caprylyl/capryl glucoside, 30% a.i., was slightly irritating to rabbit skin in studies for which the details were not provided. APGs of varying chain length (C8/10 to C12/16; 15-70% a.i.) demonstrated a structure-response relationship, with irritation potential decreasing with increasing chain length, and, independent of the degree of polymerization, the irritation was mostly concentration-dependent. The primary dermal irritation indices (PDIIs) ranged from 0.0 to 4.6 in rabbits. (A PDII of 2 was considered a positive responder).

In clinical studies, the dermal irritation of decyl, lauryl, and coco-glucosides was evaluated in epicutaneous patch (2.0% a.i.) and soap chamber tests (1.0% a.i.), and decyl glucoside was evaluated in an SIOPT (0.5% a.i.). At most, these ingredients were slightly irritating.

Glucosides with alkyl chain lengths ranging from C8-C10 to >C18, as well as a C18 branched glucoside, were evaluated in both the guinea pig maximization test (GPMT), at concentrations of 1.25-10% for intradermal induction, 5-100% for epidermal induction, and 2.5-50% for challenge, and the local lymph node assay (LLNA) at concentrations of 1.25-50%. None of the glucosides tested were irritants or sensitizers in the GPMT, but the LLNA indicated that one C12-C18 glucoside, C14 glucoside, and C18 branched glucoside may cause skin sensitization at concentrations of 8.4%, 5.9%, and 0.43%, respectively. In the LLNAs, irritation was observed with in one assay with C14 glucoside at all concentrations (1.25-10%) and C18 branched glucoside at all concentrations (2.5-50%). The sensitization potential of C12/16 APG was evaluated in studies in guinea pigs using the Buehler method (test concentrations of 20%) and the Magnusson-Kligman protocol (1, 60, and 10% used for intracutaneous induction, epidermal induction, and epidermal challenge respectively). C12/16 APG was not a sensitizer in the Buehler or Magnusson-Kligman studies.

In clinical testing, the sensitization potential of 0.5, 0.75, and 1.8% a.i. decyl glucoside (in formulation), 5% a.i. aq. decyl and lauryl glucoside and 1% a.i. aq. coco-glucoside was evaluated in a human repeated insult patch test (HRIPT). These ingredients were not irritating or sensitizing.

Case Studies

Decyl Glucoside

Case studies with reactions to antiseptic, hair, and sunscreen products that contain decyl glucoside are described in published literature.[1,28-32] Subsequent patch testing with decyl glucoside at 0.5-10% had positive results in these cases. Patch testing with other glucosides also produced positive results in these patients.

Ocular Irritation

Ocular irritation studies are summarized in Table 5. In alternative system studies for ocular irritation, the irritation potential of 0.6-3.0% a.i. decyl, lauryl, and coco-glucosides, and of C10-16 alkyl glucosides (pH 7, 11.5; concentration not stated), were non to slightly irritating. Caprylyl/capryl glucoside (concentration not stated) was highly irritating in a hen's egg test-chorioallantoic membrane (HET-CAM) assay. In a HET-CAM study with APGs of varying proportions of alkyl chain length, the ocular irritation potential increased with the increased proportion of shorter-chain APGs. In studies using rabbits, neutralized lauryl glucoside produced slight ocular reactions. Caprylyl/capryl glucoside was severely irritating to rabbit eyes when tested undiluted; the irritation threshold value was 10% for 30% a.i. caprylyl/capryl glucoside and 5% for 60% a.i. caprylyl/capryl glucoside.

SUMMARY

The 19 alkyl glucosides reviewed in this safety assessment are ingredients that consist of anomerically-alkyl-substituted D-glycopyranosides; alkyl substituents range from 2 to 22 carbons in length and the D-glycopyranosides consist of glucose-type mono-, di-, tri-, oligo-, or poly-saccharides. The alkyl glucosides are synthesized by the alcoholysis of glucose and polysaccharides under acidic conditions.

While most of these glucosides are reported to function in cosmetics as surfactants; a few are reported to function as skin conditioning agents, hair conditioning agents, or emulsion stabilizers. In 2011, decyl glucoside was reported to be used in 492 cosmetic formulations, 421 of which are rinse-offs. The most frequently used glucoside in leave-on formulations is cetearyl glucoside, with 445 of 477 uses being in leave-on formulations. Lauryl glucoside has the highest leave-on concentration of use at 8%; this leave-on use is in a hair color spray. It also is reported to have the highest leave-on concentration of use that involves dermal contact, and that concentration is 5%. Decyl glucoside has the highest rinse-off concentration of use, at 33%.

In an in vitro dermal absorption study using human skin samples, the mean absorbed dose of 10% caprylyl/capryl glucoside was 0.01%. In an oral study in which female mice were dosed by gavage with a 5% aq. solution of caprylyl [U-^{14}C]glucoside, the highest levels of radioactivity at 2 h after dosing were found in the stomach, intestines, liver, and kidneys. The radioactivity in the stomach was primarily unchanged substrate, while only a trace amount found in the liver was unchanged. Labeled glucose was found in all of these organs. In a feeding study in rats in which dietary sucrose was replaced with 10 or 20% ethyl glucoside for 39 days, 60-90% of the ingested ethyl glucoside was recovered in the urine.

In single dose dermal studies with caprylyl/capryl glucoside and C10-16 alkyl glucoside (both 50% a.i., n:1.6) in rabbits, the LD_{50} was greater than the 2 g/kg dose administered. In oral studies with the same test substances, none of the mice dosed with 2 g/kg caprylyl glucoside and none of the rats dosed with 5 g/kg C10-16 alkyl glucoside died during the study.

In 2-wk repeated dose dermal studies in rabbits with 60% active caprylyl/capryl glucoside, occlusive applications produced testicular effects, while non-occlusive application did not. In the two occlusive studies, one with 0.09 and 1.8 g a.i./kg and the other with 0.14-1.25 g a.i./kg, an NOEL for testicular effects could not be established; the NOEL for microscopic effects in the epididymides, prostate, and vesicular glands was 0.14 g a.i./kg. In the non-occlusive study, the NOEL for systemic toxicity was 0.18 g a.i./kg caprylyl/capryl glucoside. It was not clear if the effects were test-article related, due to inflammation, or due to stress of the occlusive procedure and resulting irritation and weight loss. Severe dermal irritation was observed in both occlusive studies, while slight to moderate irritation was reported in the non-occlusive study.

In oral repeated dose toxicity studies, moderately-dilated renal tubules were observed in 3 of 6 rats fed 20% ethyl glucoside for 39 days, but in none of the rats fed 10% ethyl glucoside. Kidney weights were statistically significantly increased in the test animals. In rats dosed orally with 0.25-1 g/kg C12/16 APG for 13 wks, reversible irritation and ulceration of the stomach mucosa was observed, but there was no systemic toxicity reported for any group.

Lauryl glucoside, 0.1-1 g/kg by gavage, did not produce adverse reproductive or developmental effects when given to female Sprague-Dawley rats on days 6-15 of gestation or when administered from 2 wks prior to mating to 4 days after delivery. Lauryl glucoside, 0.1-10,000 nmol, did not have any activity in in vitro estrogenicity assays.

APGs (chain length not specified), tested at 8-500 µg/l and 11-900 µg/plate in distilled water, were not mutagenic in Ames tests with or without metabolic activation. C10-16 APG, tested at concentrations of ≤160 µg/ml with and ≤16 µg/ml without metabolic activation, was not clastogenic in Chinese hamster V79 lung fibroblasts.

In dermal repeated dose (2-wk) toxicity tests using rabbits, caprylyl/capryl glucoside (60% a.i.) tested at concentrations ranging from-3.5-45% a.i. in distilled water produced severe irritation over time at all concentrations tested; in a non-occlusive study, slight dermal irritation was seen in similar testing with 3 and 9% (a.i.) caprylyl/capryl glucoside, and moderate irritation was reported with 27% a.i. after 3 days of testing. Caprylyl/capryl glucoside, 30% a.i., was slightly irritating to rabbit skin in studies for which the details were not provided. With APGs of varying chain length (C8/10 to C12/16; 15-70% a.i.), there was a structure-response relationship with irritation potential decreasing with increasing chain length, and, independent of the degree of polymerization, the irritation was concentration-dependent. The primary dermal irritation indices (PDIIs) ranged from 0.0 to 4.6 in rabbits. (A PDII of 2 was considered a positive responder). In clinical studies, the dermal irritation of decyl, lauryl, and coco-glucosides was evaluated in epicutaneous patch (2.0% a.i.) and soap chamber tests (1.0% a.i.), and decyl glucoside was evaluated in an SIOPT (0.5% a.i.). At most, these ingredients were slightly irritating.

Glucosides with alkyl chain lengths ranging from C8-C10 to >C18, as well as a C18 branched glucoside, were evaluated in both the GPMT, at concentrations of 1.25-10% for intradermal induction, 5-100% for epidermal induction, and 2.5-50% for challenge, and the LLNA at concentrations of 1.25-50%. None of the glucosides tested were irritants or sensitizers in the GPMT, but the LLNA indicated that one C12-C18 glucoside, C14 glucoside, and C18 branched glucoside may cause skin sensitization at concentrations of 8.4%, 5.9%, and 0.43%, respectively. In the LLNAs, irritation was observed with in one assay with C14 glucoside at all concentrations (1.25-10%) and C18 branched glucoside at all concentrations (2.5-50%). The sensitization potential of C12/16 APG was evaluated in studies in guinea pigs using the Buehler method (test concentrations of 20%) and the Magnusson-Kligman protocol (1, 60, and 10% used for intracutaneous induction, epidermal induction, and epidermal challenge respectively). C12/16 APG was not a sensitizer in the Buehler or Magnusson-Kligman studies. In clinical testing, the sensitization potential of 0.5, 0.75, and 1.8% a.i. decyl glucoside (in formulation), 5% a.i. aq. decyl and lauryl glucoside, and 1% a.i. aq. coco-glucoside was evaluated in HRIPTs. These ingredients were not irritating or sensitizing.

In alternative system studies for ocular irritation, the irritation potential of 0.6-3.0% a.i. decyl lauryl, and coco-glucosides, and of C10-16 alkyl glucosides (pH 7, 11.5; concentration not stated), were non to slightly irritating. Caprylyl/capryl glucoside (concentration not stated) was highly irritating in a HET-CAM assay. In a HET-CAM study with APGs of varying proportions of alkyl chain length, the ocular irritation potential increased with the increased proportion of shorter-chain APGs. In studies using rabbits, neutralized lauryl glucoside produced slight ocular reactions. Caprylyl/capryl glucoside was severely irritating to rabbit eyes when tested undiluted; the irritation threshold value was 10% for 30% a.i. caprylyl/capryl glucoside and 5% for 60% a.i. caprylyl/capryl glucoside.

DISCUSSION

Alkyl glucosides, like many other cosmetic ingredients, are provided to formulators at less than 100% active substance. The CIR Expert Panel confirmed that the use concentrations, as given in an industry survey, were as active ingredient.

The Panel was satisfied that sensitization data are adequate. The highest leave-on concentration of use that involves dermal contact is 5% lauryl glucoside. Irritation and sensitization data on lauryl and decyl glucoside at 5% a.i., indicating no sensitization reactions, were reported.

The Panel was concerned, however, that the potential exists for dermal irritation with the use of products formulated using decyl glucoside or other alkyl glucosides. Therefore, the Panel specified that products must be formulated to be non-irritating.

In dermal repeated dose studies of caprylyl/capryl glucoside using an occlusive wrap, effects on the testes and accessory sex organs of rabbits were observed. These effects were not reported with a non-occlusive application. In the experience of the Panel, changes in these organs can be observed during stress, and it was the view of the Panel that these effects were due to the stress of the study and were not indications of toxicity of the test ingredient.

The Panel noted there were gaps in the available safety data for many of the alkyl glucosides included in this group. These ingredients have similar chemical structures and are used in similar ways in cosmetics, which suggested that they would have similar structure activity relationships. The Panel determined, therefore, that it was appropriate to extrapolate the existing data, including the data from previous CIR assessments on fatty alcohols, to address all the alkyl glucosides

included in this safety assessment. The Expert Panel recognized that the alkyl glucosides can enhance the penetration of other ingredients through the skin. The Panel cautioned that care should be taken in formulating cosmetic products that may contain these ingredients in combination with any ingredients for which safety was based on their lack of dermal absorption data, or when dermal absorption was a concern.

Because some of the alkyl glucosides can be used in products that may be sprayed, the Panel discussed the issue of incidental inhalation exposure. In the absence of inhalation data, the Panel considered oral toxicity data which suggested little systemic toxicity for alkyl glucosides.., The Panel noted that 95% – 99% of droplets/particles produced in cosmetic aerosols would not be respirable to any appreciable amount. Coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, this information suggested that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic toxic effects.

CONCLUSION

The CIR Expert Panel concluded that the 19 alkyl glucosides listed below are safe in the present practices of use and concentration when formulated to be non-irritating.

Decyl Glucoside
Arachidyl Glucoside
Butyl Glucoside*
C10-16 Alkyl Glucoside*
C12-18 Alkyl Glucoside*
C12-20 Alkyl Glucoside
C20-22 Alkyl Glucoside*
Caprylyl/Capryl Glucoside
Caprylyl Glucoside
Cetearyl Glucoside
Coco-Glucoside
Ethyl Glucoside
Hexadecyl D-Glucoside
Isostearyl Glucoside*
Lauryl Glucoside
Myristyl Glucoside
Octadecyl D-Glucoside
Octyldodecyl Glucoside*
Undecyl Glucoside*

Were ingredients in this group not in current use (as indicated by *) to be used in the future, the expectation is that they would be used at concentrations comparable to others in this group and be formulated to be non-irritating.

TABLES

Table 1. Definitions, functions, and structures of the alkyl glucosides in this safety assessment.

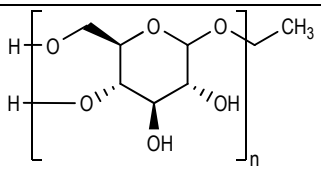
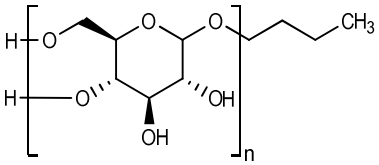
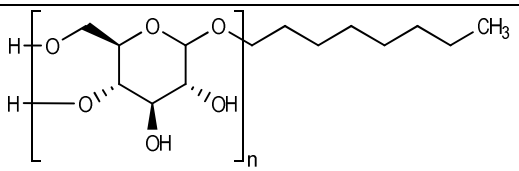
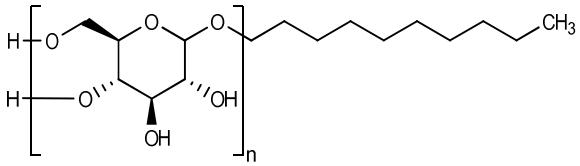
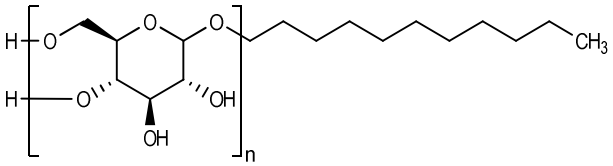
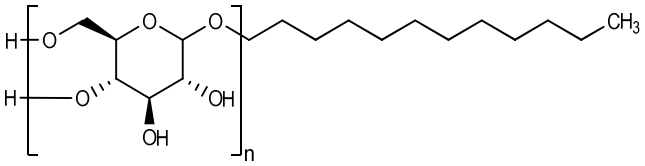
Ingredient CAS No.	Definition	Reported Function(s)[4]	Formula/structure
Ethyl Glucoside 30285-48-4	Ethyl Glucoside is the product obtained from the condensation of ethyl alcohol and glucose.	Skin-Conditioning Agents - Humectant	
Butyl Glucoside 5391-18-4 41444-57-9	Butyl Glucoside is the product obtained by the condensation of butyl alcohol with glucose.	Surfactants - Cleansing Agents	
Caprylyl Glucoside 29836-26-8	Caprylyl Glucoside is the product obtained by the condensation of caprylic alcohol with glucose.	Surfactants - Cleansing Agents	
Decyl Glucoside 58846-77-8 68515-73-1 141464-42-8	Decyl Glucoside is the product obtained from the condensation of decyl alcohol with glucose.	Surfactants - Cleansing Agents	
Undecyl Glucoside 98283-67-1	Undecyl Glucoside is the product obtained by the condensation of undecyl alcohol with glucose.	Surfactants - Cleansing Agents	
Lauryl Glucoside 27836-64-2 110615-47-9	Lauryl Glucoside is the product obtained by the condensation of lauryl alcohol with glucose.	Surfactants - Cleansing Agents	
Myristyl Glucoside 54549-26-7	Myristyl Glucoside is the product obtained by the condensation of myristyl alcohol with glucose.	Surfactants - Cleansing Agents	

Table 1. Definitions, functions, and structures of the alkyl glucosides in this safety assessment.

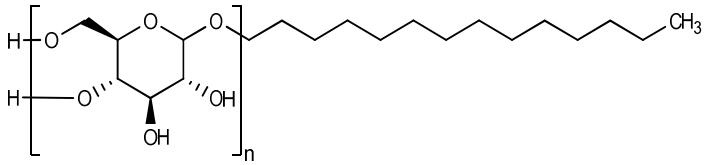
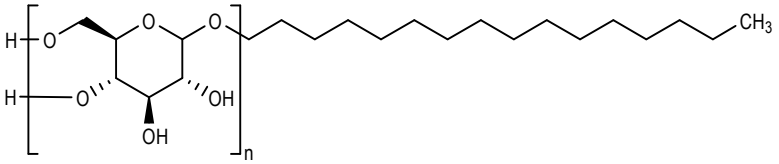
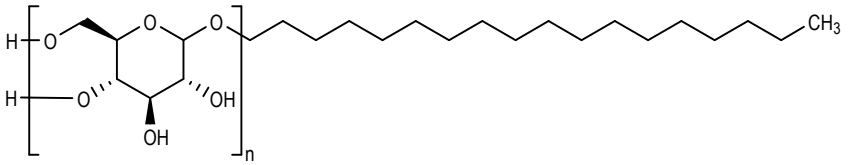
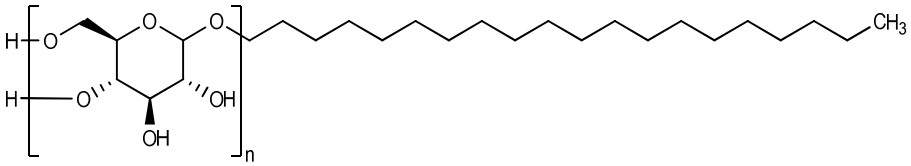
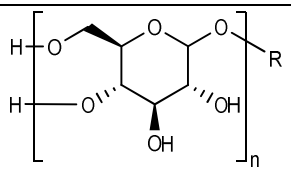
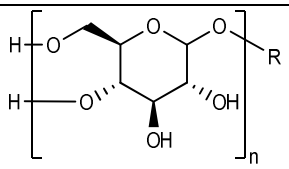
Ingredient CAS No.	Definition	Reported Function(s)[4]	Formula/structure
			
Hexadecyl D-Glucoside (VCRP name)	Hexadecyl D-Glucoside (Cetyl Glucoside) is the product obtained by the condensation of cetyl alcohol with glucose.	this ingredient is not listed in the Dictionary	
Octadecyl D-Glucoside (VCRP name)	Octadecyl D-Glucoside (Stearyl Glucoside) is the product obtained by the condensation of stearyl alcohol with glucose.	this ingredient is not listed in the Dictionary	
Arachidyl Glucoside 144982-05-8	Arachidyl Glucoside is the product obtained by the condensation of Arachidyl Alcohol with glucose.	Surfactants - Cleansing Agents	
Mixtures			
Caprylyl/ Capryl Glucoside 68515-73-1	Caprylyl/Capryl Glucoside is the product obtained by the condensation of a mixture of caprylic and decyl alcohols with glucose.	Surfactants - Cleansing Agents	 wherein R = an alkyl chain 8 or 10 carbons long
C10-16 Alkyl Glucoside 110615-47-9	C10-16 Alkyl Glucoside is the product obtained by the condensation of C10-16 alcohols with glucose.	Surfactants - Emulsifying Agents	 wherein R = an alkyl chain 10 to 16 carbons long

Table 1. Definitions, functions, and structures of the alkyl glucosides in this safety assessment.

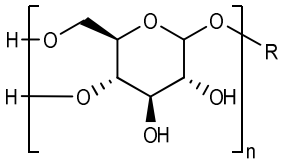
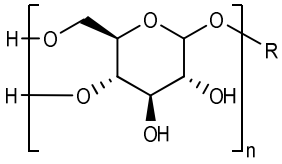
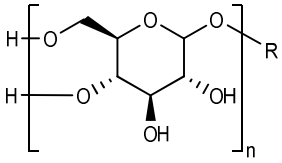
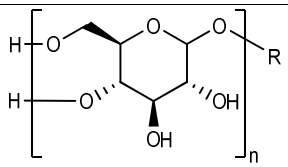
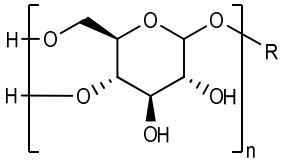
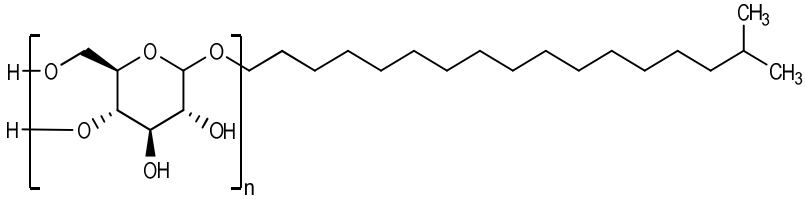
Ingredient CAS No.	Definition	Reported Function(s)[4]	Formula/structure
C12-18 Alkyl Glucoside	C12-18 Alkyl Glucoside is the product obtained by the condensation of C12-18 alcohols with glucose.	Emulsion Stabilizers	 wherein R = an alkyl chain 12 to 18 carbons long
C12-20 Alkyl Glucoside	C12-20 Alkyl Glucoside is the product obtained by the condensation of C12-20 alcohols with glucose.	Surfactants - Emulsifying Agents	 wherein R = an alkyl chain 12 to 20 carbons long
Cetearyl Glucoside	Cetearyl Glucoside is the product obtained by the condensation of cetearyl alcohol with glucose.	Surfactants - Emulsifying Agents	 wherein R = an alkyl chain 16 or 18 carbons long
C20-22 Alkyl Glucoside	C20-22 Alkyl Glucoside is the product obtained by the condensation of C20-22 alcohols with glucose.		 wherein R = an alkyl chain 20 to 22 carbons long
Coco-Glucoside	Coco-Glucoside is the product obtained by the condensation of coconut alcohol with glucose.	Surfactants - Cleansing Agents	 wherein R = alkyl chain residue of fatty alcohols derived from Coconut Acid
Branched			
Isostearyl Glucoside 200413-69-0	Isostearyl Glucoside is the product obtained by the condensation of isostearyl alcohol with glucose.	Surfactants - Emulsifying Agents	one example of an "iso" 
Octyldodecyl Glucoside	Octyldodecyl Glucoside is the product obtained by the reaction of octyldodecanol with glucose.	Surfactants - Emulsifying Agents	

Table 1. Definitions, functions, and structures of the alkyl glucosides in this safety assessment.

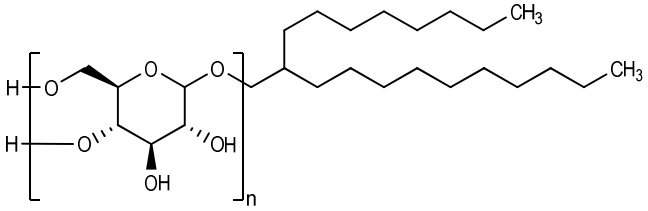
Ingredient CAS No.	Definition	Reported Function(s)[4]	Formula/structure
			

Table 2. Chemical and physical properties

Property	Description	Reference
	Decyl Glucoside	
appearance	cloudy, viscous aq. solution (as Plantacare 2000 UP) (of poly) light yellow aq. solution (as APG 0810) (of poly)	33 34
molecular weight	340.2 (of mono) 390 g/mol (as Plantacare 2000) (of poly)	35 33
active substance	51-55% (as Plantacare 2000 UP) (of poly) ≥50% (as APG 0810) (of poly)	33 34
boiling point	467.5°C (of mono)	35
melting point	135.6°C (of mono)	36
critical micelle concentration	2-3 mM (of poly, specifically the maltopyranoside)	12
viscosity	1000-6000 mPas (20°C) aq. solution (as Plantacare 2000 UP) (of poly) ≤500 mPas (20°C) aq. solution (as APG 0810, a polyglucoside) (of poly)	33 34
density	1.14 g/cm^3 (at 20°C) (of mono)	35
log P	2.092 (at 25°C) (of mono)	35
may contain (as Plantacare 2000 UP): magnesium oxide free fatty alcohol sulfate ash (as APG 0810): free fatty acid ash	 max. 500 ppm (of poly) max. 1.0% (of poly) max. 3.0% (of poly) ≤1% (of poly) ≤2% (of poly)	37 34
	Ethyl Glucoside (mono)	
molecular weight	208.21	35
boiling point	395.1°C	35
melting point	176-179°C	38
density	1.40 g/cm^3 (at 20°C)	35
log P	-2.159 (at 25°C)	35
	Butyl Glucoside (mono)	
molecular weight	236.26	35
boiling point	412.0°C	35
melting point	86-87°C	39
density	1.30 g/cm^3 (at 20°C)	35
log P	-1.151 (at 25°C)	35
	Caprylyl Glucoside	
appearance	white solid yellowish, slightly cloudy and viscous aq. solution (as Plantacare 810 UP) (of poly)	40 41
molecular weight	292.37	40
active substance	62-65% (as Plantacare 810 UP) (of poly)	
boiling point	454.1°C	35
melting point	65-99° (sic)	40
critical micelle concentration	20-25 mM	12
density	1.18 g/cm^3 (at 20°C)	35
log P	0.887 (at 25°C)	35
may contain (as Plantacare 810 UP): fatty alcohol	 ≤0.7% (of poly)	41

Table 2. Chemical and physical properties

Property	Description	Reference
	Undecyl Glucoside (mono)	
molecular weight	334.45	35
boiling point	487.8°C	35
density	1.13 g/cm^3 (at 20°C)	35
log P	2.642 (at 25°C)	35
	Lauryl Glucoside	
appearance	viscous pale yellow aq. solution (as APG 1214,) (of poly)	34
molecular weight	343.2 348.47 (of mono) 420 (as Plantacare 1200 UP) (of poly)	16 35 42
active substance	50-53% (as APG 1214 and as Plantacare 1200 UP) (of poly)	34,42
boiling point	499.1°C (of mono)	35
critical micelle concentration	0.13 mM (of poly, specifically the maltopyranoside)	12
viscosity	≥2000 mPas (20°C) aq. solution (as APG 1214) (of poly)	34
density	1.12 g/cm^3 (at 20°C) (of mono)	35
log P	2.925 (at 25°C) (of mono)	35
may contain (as Plantacare 12900 UP)		42
fatty alcohol	≤0.8% (of poly)	
ash	≤2%(of poly)	
(as APG 1214):		34
free fatty acid	≤1% (of poly)	
ash	≤2%(of poly)	
	Myristyl Glucoside (mono)	
molecular weight	376.53	35
boiling point	521.5°C	35
density	1.09 g/cm^3 (at 20°C)	35
log P	4.218 (at 25°C)	35
	Arachidyl Glucoside (mono)	
molecular weight	460.69	35
boiling point	586.8°C	35
density	1.04 g/cm^3 (at 20°C)	35
log P	7.406 (at 25°C)	35
	Coco-Glucoside (poly)	
appearance	cloudy, viscous aq. solution (as Plantacare 818 UP) cloudy, viscous pale yellow aq. solution (as APG 0814, a polyglucoside)	43 34
% active	51-53% (as Plantacare 818 UP) ≥50% (as APG 0814, a polyglucoside)	43 34
viscosity	2500-6000 mPas (20°C) aq. solution (as Plantacare 818 UP) ≤2000 aq. solution (as APG 0814, a polyglucoside)	43 34
may contain (as Plantacare 818 UP)		43
magnesium oxide	max. 500 ppm magnesium	
free fatty alcohol	max. 1.0%	
sulfate ash	max. 3.0%	
may contain (as APG 0814):		34
free fatty acid	≤1%	
ash	≤2%	

Table 3a. Frequency and concentration of use according to duration and type of exposure

	Decyl Glucoside		Arachidyl Glucoside		C12-20 Alkyl Glucoside	
	# of Uses[5]	*Max Concs of Use (%)*[6]	*# of Uses*[5]	*Max. Concs of Use (%)*[6]	*# of Uses*[5]	*Max. Concs. of Use (%)*[6]
Totals*	**492**	**0.002-33**[#]	**75**	**0.08-0.6**	**54**	**0.1-1**
Duration of Use						
Leave-On	*62*	*0.002-2*	*73*	*0.08-0.6*	*42*	*0.2-1*
Rinse Off	*421*	*0.3-33*	*2*	*0.5*	*12*	*0.1*
Diluted for (Bath) Use	*9*	*0.5-1*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	12	0.02-6	3	0.08	2	0.2-0.8
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Sprays	5[a]	0.2-0.8[a]	13[a]	0.2-0.5[a]	2[a]	0.2-0.5[a]
Incidental Inhalation-Powders	1	NR	NR	NR	NR	NR
Dermal Contact	379	0.002-33	75	0.08-0.6	48	0.1-1
Deodorant (underarm)	NR	NR	NR	NR	NR	0.6[b]
Hair - Non-Coloring	94	0.2-7	NR	0.5	6	1
Hair-Coloring	9	2-8	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	208	0.3-11	NR	NR	NR	NR
Baby Products	25	NR	NR	NR	NR	NR

	Caprylyl/Capryl Glucoside		Caprylyl Glucoside		Cetearyl Glucoside	
	# of Uses[5]	*Max. Concs of Use (%)*[44]	*# of Uses*[5]	*Max. Concs of Use (%)*[44]	*# of Uses*[5]	*Max Conc of Use (%)*[44]
Totals*	**58**	**0.06-3**	**NR**	**4**	**477**	**0.03-3**
Duration of Use						
Leave-On	*27*	*0.06-0.8*	*NR*	*4*	*445*	*0.2-2*
Rinse Off	*31*	*0.3-3*	*NR*	*NR*	*31*	*0.03-3*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*1*	*NR*
Exposure Type						
Eye Area	6	0.2-0.3	NR	NR	61	0.6-2
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Sprays	1[a]	0.3[a]	NR	NR	29[a]	0.2-0.6[a]
Incidental Inhalation-Powders	NR	NR	NR	NR	2	NR
Dermal Contact	51	0.06-0.9	NR	NR	466	0.03-3
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	7	0.3-3	NR	4	4	0.3-0.6
Hair-Coloring	NR	3	NR	NR	NR	0.2
Nail	NR	NR	NR	NR	2	NR
Mucous Membrane	6	NR	NR	NR	6	0.03
Baby Products	NR	0.06	NR	NR	3	NR

	Coco-Glucoside		Ethyl Glucoside		Lauryl Glucoside	
	# of Uses[5]	*Max. Conc of Use (%)*[44]	*# of Uses*[5]	*Max. Conc of Use (%)*[44]	*# of Uses*[5]	*Max. Conc of Use (%)*[44]
Totals*	**350**	**0.006-15**	**24**	**0.02-0.3**	**399**	**0.03-10**
Duration of Use						
Leave-On	*42*	*0.006-2*	*14*	*0.02-0.3*	22	0.03-8
Rinse Off	*294*	*0.2-15*	*10*	*0.02-0.05*	347	0.3-10
Diluted for (Bath) Use	*14*	*NR*	*NR*	*NR*	30	0.3-4
Exposure Type						
Eye Area	6	2-3	2	0.02	NR	5
Incidental Ingestion	NR	0.5	NR	NR	NR	NR
Incidental Inhalation-Sprays	1	0.4-1[a]	NR	NR	NR	8
Incidental Inhalation-Powders	NR	NR	NR	NR	NR	NR
Dermal Contact	275	0.006-15	24	0.02-0.3	308	0.03-10
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	59	0.2-8	NR	NR	70	0.4-5
Hair-Coloring	16	0.3-5	NR	NR	15	0.3-8
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	177	0.4-15	1	NR	218	0.3-8
Baby Products	11	NR	NR	NR	5	NR

Table 3a. Frequency and concentration of use according to duration and type of exposure

	Myristyl Glucoside		Hexadecyl D-Glucoside**		Octadecyl D-Glucoside**	
	# of Uses[5]	*Max. Conc of Use (%)*[6]	*# of Uses*[5]	*Max Conc of Use (%)*[45]	*# of Uses*[5]	*Max. Conc of Use (%)*[45]
Totals*	**5**	**0.4-0.6**	**1**	**3%**	**1**	**NR**
Duration of Use						
Leave-On	*4*	*0.4-0.6*	*1*	*3*	*1*	*NR*
Rinse Off	*1*	*NR*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	2	0.4	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Sprays	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powders	NR	NR	NR	NR	NR	NR
Dermal Contact	5	0.4-0.6	1	3	1	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR

* Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types my not equal the sum of total uses.

** These ingredients are included in the VCRP, but are not listed in the *International Cosmetic Ingredient Dictionary and Handbook*

[#]Concentration of use is provided as active ingredient

[a] Includes suntan products, in that it is not known whether or not the reported product is a spray.

[b] It is not known whether or not the product is a spray.

NR – none reported

Table 3b. Ingredients Not Reported to be Used

Butyl Glucoside
C10-16 Alkyl Glucoside
C12-18 Alkyl Glucoside
C20-22 Alkyl Glucoside
Isostearyl Glucoside
Octyldodecyl Glucoside
Undecyl Glucoside

Table 4. Skin irritation and sensitization studies

Ingredient/Chain Length	% a.i.; n; conc. tested	Test Population	Method	Results	Reference
			IRRITATION STUDIES		
			NON-HUMAN		
Caprylyl/Capryl Glucoside	60% a.i.; 0.9 and 1.8 g a.i./kg applied (22.5 and 45 w/v%, respectively) in distilled water	6 male and female NZW rabbits/group	10 occlusive 6-h applications made over a 2-wk period; 4 ml/kg applied	slight irritation was observed on day 1 after the initial dose; severe dermal irritation was observed in males and females of both test groups by days 5-6	21
Caprylyl/Capryl Glucoside	60% a.i.; 0.06, 0.18 and 0.54 g a.i./kg applied (3, 9, and 27 % a.i., respectively) in distilled water	6 male rabbits/group	10 non-occlusive 6-h applications made over a 2-wk period;; 2 ml applied to intact skin	slight dermal irritation in all groups after initiation of dosing; moderate irritation in the high-dose group after 3 days	26
Caprylyl/Capryl Glucoside	60% a.i.; 0.14, 0.41 and 1.25 g a.i./kg applied (3.5 10.4, and 31.1 % a.i., respectively) in distilled water	6 male NZW rabbits/ group	10 occlusive applications made over a 2-wk period	dermal irritation progressed from slight to severe with time in all test groups; slight to moderate irritation was observed in controls	24
Caprylyl/Capryl Glucoside	30% a.i.	rabbits; no. not specified	not provided	slightly irritating,; PII 0-2	46-48
C8/10 APG	15% a.i	5 rabbits	4 h application; semi-occlusive patch	PDII=0.0	20
C8/10 APG	35% a.i.; n:1.6	3 rabbits	4 h application; semi-occlusive patch	PDII = 1.3; no signs of systemic toxicity; edema was reported in 2/3 rabbits	20
C8/10 APG	70% a.i.; n:1.6	3 rabbits	4 h application; semi-occlusive patch	PDII = 0.8; no signs of systemic toxicity	20
C10/16 APG	20% a.i.; n:1.4	4 rabbits	4 h application; occlusive patch	PDII=0.4; no signs of systemic toxicity	20
C10/16 APG	60% a.i.; n:1.4	4 rabbits	4 h application; occlusive patch	PDII=4.6; erythema and edema in all animals; 24/48/72 h mean erythema score-2.9, mean edema score-2.1	20
C12/16 APG	50% a.i.; n:1.4	3 rabbits	4 h application; semi-occlusive patch	PDII=3.7; no signs of systemic toxicity; erythema and edema in all animals; 24/48/72 h mean erythema score-2.2, mean edema score-1.6	20
C12/16 APG	50% a.i.; n:1.4	3 rabbits	4 h application; semi-occlusive patch	PDII=3.0; no signs of systemic toxicity; erythema in all animals and edema in 1 animal; 24/48/72 h mean erythema score-2.1, mean edema score-0.9	20
C12/16 APG	50% a.i.; n:1.4	3 rabbits	4 h application; semi-occlusive patch	PDII=3.0; no signs of systemic toxicity; erythema in all animals and edema in 1 animal; 24/48/72 h mean erythema score-1.9, mean edema score-1.1	20
C8/10 + C12/16 APG	C8/10, 21% a.i. C12/16, 35% a.i.	3 rabbits	4 h application; semi-occlusive patch	PDII=2.7; erythema and edema in all animals; 24/48/72 h mean erythema score-1.8, mean edema score-0.8	20

Table 4. Skin irritation and sensitization studies

Ingredient/Chain Length	% a.i.; n; conc. tested	Test Population	Method	Results	Reference
			HUMAN		
Decyl Glucoside	2.0% a.i., pH 6.5	20 subjects	epicutaneous patch test; 75 µl, 24 h occlusive application	very slightly irritating	[49]
Decyl Glucoside	1.0% a.i., pH 6.5	22 subjects	soap chamber test; 100 µl applied occlusively to the ventral for 24 h on day 1 and 6 h on days 2-5	slightly irritating	[49]
Decyl Glucoside	a.i. not stated; tested at 0.5% aq.	105 subjects; 14.3% were atopic patients	SIOPT; 40 µl was applied for 48 h using Haye's test chambers	AII=0.046; non-irritating	[50]
Lauryl Glucoside	2.0% a.i., pH 6.5	20 subjects	epicutaneous patch test; 75 µl, 24 h occlusive application	slightly irritating	[49]
Lauryl Glucoside	1.0% a.i., pH 6.5	22 subjects	soap chamber test; 100 µl applied occlusively to the ventral for 24 h on day 1 and 6 h on days 2-5	slightly irritating	[49]
Lauryl Glucoside	a.i. not stated; tested at 0.5% aq.	105 subjects; 14.3% were atopic patients	SIOPT; 40 µl was applied for 48 h using Haye's test chambers	AII=0.046; non-irritating	[50]
Coco-Glucoside	2.0% a.i., pH 6.5	20 subjects	epicutaneous patch test; 75 µl, 24 h occlusive application	slightly irritating	[49]
Coco-Glucoside	1.0% a.i., pH 6.5	22 subjects	soap chamber test; 100 µl applied occlusively to the ventral forearm for 24 h on day 1 and 6 h on days 2-5	slightly irritating	[49]
			SENSITIZATION		
			NON-HUMAN		
C8-C10 glucoside	a.i. not stated; tested at 1.25-25% in acetone/olive oil (4:1)	4-5 CBA/j mice	LLNA; 25 µl/ear	not an irritant or a sensitizer	[51]
C8-C10 glucoside	a.i. not stated; tested at 5% - intraderm induction 5% - epiderm induction 2.5 and 5% - challenge	guinea pigs; 10 treated, 5 controls	GPMT with FCA and SLS; 0.5 ml applied to an 8 cm^2 area under an occlusive induction patch; at challenge, 0.2 ml was applied to a 4 cm^2 area	not an irritant or sensitizer	[51]
C10-C14 glucoside	a.i. not stated; tested at 1.25-5% in DMF	4-5 CBA/j mice	LLNA; 25 µl/ear	not an irritant or sensitizer	[51]
C10-C14 glucoside	a.i. not stated; tested at 5% - intraderm induction 5% - epiderm induction 2.5 and 5% - challenge	guinea pigs; 10 treated, 5 controls	GPMT with FCA and SLS; 0.5 ml applied to an 8 cm^2 area under an occlusive induction patch; at challenge, 0.2 ml was applied to a 4 cm^2 area	not an irritant or sensitizer	[51]
C12/16 APG (may be similar to C12-18 alkyl glucoside)	a.i. not provided	20 guinea pigs	Buehler method; 20% tested at induction and challenge	not a sensitizer; one very weak reaction during induction and challenge for one guinea pig	[52]
C12/16 APG (may be similar to C12-18 alkyl glucoside)	a.i. not provided	20 guinea pigs	Magnusson-Kligman study; 1% used for intracutaneous and 60% for epidermal induction; 10% for epidermal challenge	not a sensitizer; no positive reactions	[52]

Table 4. Skin irritation and sensitization studies

Ingredient/Chain Length	% a.i.; n; conc. tested	Test Population	Method	Results	Reference
C12-C18 glucoside (granules)	a.i. not stated; tested at 2.5-10% in DMF	4-5 CBA/j mice	LLNA; 25 µl/ear	not an irritant or sensitizer	[51]
C12-C18 glucoside (granules)	a.i. not stated; tested at 10% - intraderm induction 50% - epiderm induction 5 and 10% - challenge	guinea pigs; 10 treated, 5 controls	GPMT with FCA and SLS; 0.5 ml applied to an 8 cm^2 area under an occlusive induction patch; at challenge, 0.2 ml was applied to a 4 cm^2 area	not an irritant or sensitizer	[51]
C12-C18 glucoside (flakes)	a.i. not stated; tested at 1.25-10% in DMF	4-5 CBA/j mice	LLNA; 25 µl/ear	EC3=8.4%, may cause skin sensitization	[51]
C12-C18 glucoside (flakes)	a.i. not stated; tested at 10% - intraderm induction 50% - epiderm induction 5 and 10% - challenge	guinea pigs; 10 treated, 5 controls	GPMT with FCA and SLS; 0.5 ml applied to an 8 cm^2 area under an occlusive induction patch; at challenge, 0.2 ml was applied to a 4 cm^2 area	not an irritant or sensitizer	[51]
C14 glucoside	a.i. not stated; tested at 1.25-10% in DMF	4-5 CBA/j mice	LLNA; 25 µl/ear	all concentrations were irritants (based on ear thickness); EC3=5.9%, may cause skin sensitization	[51]
C14 glucoside	a.i. not stated; tested at 1.25%-intraderm induction 50% - epiderm induction 25 and 50% - challenge	guinea pigs; 10 treated, 5 controls	GPMT with FCA and SLS; 0.5 ml applied to an 8 cm^2 area under an occlusive induction patch; at challenge, 0.2 ml was applied to a 4 cm^2 area	not an irritant or sensitizer	[51]
C16-C18 glucoside	a.i. not stated; tested at 2.5-10% in DMF	4-5 CBA/j mice	LLNA; 25 µl/ear	not an irritant or sensitizer	[51]
C16-C18 glucoside	a.i. not stated; tested at 10% - intraderm induction 10% - epiderm induction 5 and 10% - challenge	guinea pigs; 10 treated, 5 controls	GPMT with FCA and SLS; 0.5 ml applied to an 8 cm^2 area under an occlusive induction patch; at challenge, 0.2 ml was applied to a 4 cm^2 area	not an irritant or sensitizer	[51]
>C18 glucoside	a.i. not stated; tested at 2.5-10% in DMF	4-5 CBA/j mice	LLNA; 25 µl/ear	not an irritant or sensitizer	[51]
>C18 glucoside	a.i. not stated; tested at 5% - intraderm induction 10% - epiderm induction 2.5 and 5% - challenge	guinea pigs; 10 treated, 5 controls	GPMT with FCA and SLS; 0.5 ml applied to an 8 cm^2 area under an occlusive induction patch; at challenge, 0.2 ml was applied to a 4 cm^2 area	not an irritant or sensitizer	[51]
C18 branched glucoside	a.i. not stated; tested at 2.5-50% in DMF	4-5 CBA/j mice	LLNA; 25 µl/ear	all concentrations were irritants (based on ear thickness); there was not a clear dose response of stimulation index vs. concentration; EC3=0.43%, may cause skin sensitization	[51]
C18 branched glucoside	a.i. not stated; tested at 2.5% - intraderm induction 100% - epiderm induction 6.25 and 12.5% - challenge	guinea pigs; 10 treated, 5 controls	GPMT with FCA and SLS; 0.5 ml applied to an 8 cm^2 area under an occlusive induction patch; at challenge, 0.2 ml was applied to a 4 cm^2 area	not an irritant or sensitizer	[51]

Table 4. Skin irritation and sensitization studies

Ingredient/Chain Length	% a.i.; n; conc. tested	Test Population	Method	Results	Reference
			HUMAN		
Decyl Glucoside	0.5% a.i. in an indoor tanning preparation	103 subjects	HRIPT; 0.2 ml applied to a 20 mm^2 Webril pad, 24-h occlusive, 3x/wk for 3 wks; 9 applications; challenge performed after 10-14 day non-treatment period	not a primary irritant or sensitizer	[53]
Decyl Glucoside	0.75% a.i. in a self-tanning formulation	107 subjects	HRIPT; 24-h semi-occlusive, 3x/wk for 3 wks; 9 applications; challenge performed after 2-wk non-treatment period	not an irritant or sensitizer	[54]
Decyl Glucoside	1.8% a.i. in a liquid foundation	103 subjects	HRIPT; 150 µl applied to a 2 cm^2 patch; 24-h semi-occlusive, 3x/wk for 3 wks; 9 applications; challenge performed after 2-wk non-treatment period	not an irritant or sensitizer	[55]
Decyl Glucoside; tested under 4 tradenames	5% a.i.	49 subjects	HRIPT; 0.2 ml, 24-h semi-occlusive; 3x/wk for 3 wks; 10 applications; challenge performed after 2-wk non-treatment period	not an irritant or a sensitizer	[56]
Lauryl Glucoside; tested under 5 tradenames	5% a.i.	49 subjects	HRIPT, as above	not an irritant or a sensitizer	[56]
Coco-Glucoside	52% a.i. diluted to 2% aq. (1% a.i. tested)	213 subjects	HRIPT; 0.2 ml, 24 h occlusive; 3x/wk for 3 wks; 9 applications; challenge performed after 2-wk non-treatment period	not an irritant or a sensitizer	[57]
C8-C10 glucoside	a.i. not stated; tested at 5% aq.	50 subjects	HRIPT; 20 µl, 9 occlusive applications, 20 µl applied to a 50 mm^2 area	irritation index during induction=0.04; no positive reactions at challenge	[51]
C10-C14 glucoside	a.i. not stated; tested at 5% aq.	50 subjects	HRIPT; 20 µl, 9 occlusive applications, 20 µl applied to a 50 mm^2 area	irritation index during induction = 0; no positive reactions at challenge	[51]
C12-C18 glucoside (granules)	a.i. not stated; tested at 5% aq.	50 subjects	HRIPT; 20 µl, 9 occlusive applications, 20 µl applied to a 50 mm^2 area	irritation index during induction = 0.10; no positive reactions at challenge	[51]
C12-C18 glucoside (flakes)	a.i. not stated; tested at 1% aq.	50 subjects	HRIPT; 20 µl, 9 occlusive applications, 20 µl applied to a 50 mm^2 area	irritation index during induction = 0.15; no positive reactions at challenge	[51]
C14 glucoside	a.i. not stated; tested at 5% aq.	50 subjects	HRIPT; 20 µl, 9 occlusive applications, 20 µl applied to a 50 mm^2 area	irritation index during induction = 0.62; no positive reactions at challenge	[51]
C16-C18 glucoside	a.i. not stated; tested at 5% aq.	50 subjects	HRIPT; 20 µl, 9 occlusive applications, 20 µl applied to a 50 mm^2 area	irritation index during induction = 0.03; no positive reactions at challenge	[51]
>C18 glucoside	a.i. not stated; tested at 5% aq.	50 subjects	HRIPT; 20 µl, 9 occlusive applications, 20 µl applied to a 50 mm^2 area	irritation index during induction = 0.21; no positive reactions at challenge	[51]
C18 branched glucoside	a.i. not stated; tested at 6%	50 subjects	HRIPT; 20 µl, 9 occlusive applications, 20 µl applied to a 50 mm^2 area	irritation index during induction = 0.04; no positive reactions at challenge	[51]

Abbreviations: a.i. – active ingredient; AII – average index of skin irritation; APG – alkyl polyglucoside; DMF – dimethyl formamide; FCA – Freund's complete adjuvant; HRIPT – human repeat insult patch test; LLNA – local lymph node assay; n – degree of polymerization; PDII – primary dermal irritation index; SIOPT – single insult occlusive patch test; SLS – sodium lauryl sulfate positive responder: irritation score = 2

Table 5. Ocular irritation studies

Ingredient/Chain Length	% a.i.; pH; conc. tested	Animals	Method	Results	Reference
ALTERNATIVE STUDIES					
Decyl Glucoside	1.0% a.i. in PBS; pH 7		RBC	not irritating	49
Decyl Glucoside	3.0% a.i.; pH 6.5 , aq. soln		HET-CAM assay	slightly irritating	49
Decyl Glucoside	0.6% a.i.; pH 7.0 , aq. soln		ocular tissue model	not irritating	49
Lauryl Glucoside	1.0% a.i. in PBS; pH 7		RBC	slightly irritating	49
Lauryl Glucoside	3.0% a.i.; pH 6 , aq. soln		HET-CAM assay	slightly irritating	49
Lauryl Glucoside	0.6% a.i.; pH 7.0, aq. soln		ocular tissue model	not irritating	49
Caprylyl/Capryl Glucoside, as C8/C10 APG	not specified		HET-CAM assay	highly irritating	20
C10-16 Alkyl Glucoside, as C10/16 APG	pH 7		HET-CAM assay	produced slight reactions	20
C10-16 Alkyl Glucoside, as C10/16 APG	pH 11.5		HET-Cam assay	produced slight reactions	20
Coco-Glucoside	1.0% a.i. in PBS; pH 7.4, aq. Soln		RBC	not irritating	49
Coco-Glucoside	3.0% a.i.; pH 6.5, aq. soln		HET-CAM assay	slightly irritating	49
Coco-Glucoside	0.6% a.i.; pH 7.0, aq. soln		ocular tissue model	not irritating	49
NON-HUMAN STUDIES					
Lauryl Glucoside, neutralized	12.5% a.i.	6 NZW rabbits	0.1 ml instilled into the conjunctival sac; eyes were not rinsed	very slight reactions, in one animal (subsided in 48 h); medium to mild conjunctival irritation was observed in all rabbits; effects were reversible within 7 days in all but one of the rabbits	20
Caprylyl/Capryl Glucoside	30% a.i.	9 rabbits	0.1 ml instilled into the conjunctival sac; eyes of 3 rabbit rinsed 20-30 sec after dosing	severely irritating; rinsing reduced the intensity and duration	47
Caprylyl/Capryl Glucoside	30% a.i.	9 rabbits	0.1 ml instilled into the conjunctival sac; eyes of 3 rabbit rinsed 20-30 sec after dosing	severely irritating; rinsing reduced the intensity and duration	46
Caprylyl/Capryl Glucoside	30% a.i.	9 rabbits	0.1 ml instilled into the conjunctival sac; eyes of 3 rabbit rinsed 20-30 sec after dosing	severely irritating	48
Caprylyl/Capryl Glucoside	30% a.i.	9 rabbits	0.1 ml instilled into the conjunctival sac; eyes of 3 rabbit rinsed 20-30 sec after dosing	severely irritating	58
Caprylyl/Capryl Glucoside	30% a.i.	9 rabbits	0.1 ml instilled into the conjunctival sac; eyes of 3 rabbit rinsed 20-30 sec after dosing	severely irritating	59
Caprylyl/Capryl Glucoside	30% a.i.; 0.1-50% tested	2 rabbits/group; 4 additional rabbits dosed w/5 and 10%	0.1 ml instilled into the conjunctival sac	0.1, 0.5, 1.0, 5.0%: non or inconsequential irritant 10%: conjunctival irritation in 6/6 at 4 h; subsided in 4/6 by 72 h; moderate irritant 20%: moderate irritant 50% substantial to severe irritant Irritation threshold determined to be 10% (v/v); equivalent to 3% solids	60

Table 5. Ocular irritation studies

Ingredient/Chain Length	% a.i.; pH; conc. tested	Animals	Method	Results	Reference
Caprylyl/Capryl Glucoside	60% a.i.	rabbits	details not provided	severely irritating	61
Caprylyl/Capryl Glucoside	60% a.i.; conc. of 0.5, 1.0, 5.0, and 10.0% tested	6 rabbits/group	0.1 ml instilled into the conjunctival sac	0.5 and1.0%: no irritation 5%: conjunctival irritation at 4 h, cleared by 72 h 10%: moderate irritation in 6/6, cleared by 72 h	62
	60% a.i.; conc. of 20 and 50.0% tested	2 rabbits/group	0.1 ml instilled into the conjunctival sac	20 and 50%: severely irritating Irritation threshold determined to be 5.0%	
Caprylyl/Capryl Glucoside	70% a.i.; 40% solution	6 rabbits/study	0.1 ml instilled into the conjunctival sac; two studies performed	moderately to highly irritating (both studies)	63
Caprylyl/Capryl Glucoside	70% a.i.	not provided	not provided; two studies performed	moderately to highly irritating (both studies)	64
Caprylyl/Capryl Glucoside	70% a.i.; 40% solution	6 rabbits	0.1 ml instilled into the conjunctival sac; two studies performed	moderately to highly irritating (both studies)	65
C12/16 APG (may be similar to C12-18 alkyl glucoside)	50% a.i, aq. Solution	4 albino rabbits	OECD Guideline 405	24/48/72 h mean scores for the cornea, conjuncti-val erythema, and iris: 0.5/4, 2.08/3, and 0.25/2, respectively; moderate to strong reactions in the conjunctivae did not completely subside within 21 days in 2 of the animals, persistent corneal effects did not subside in 1 of these rabbits	20

Abbreviations: a.i. – active ingredient; HET-CAM – hen's egg test-chorioallantoic membrane; PBS – phosphate buffered saline; RBC – red blood cell test

Table 6. Summaries of information on fatty alcohols from previous CIR reports

Ingredient	Parameter Evaluated	Outcome	Reference
n-Butyl Alcohol	ADME	can be absorbed through the lungs, gastrointestinal tract, the cornea, and the skin; mainly metabolized by alcohol dehydrogenase and eliminated rapidly from the blood; dogs given i.v. n-butyl alcohol eliminated 15% of the does in CO_2(none unchanged) and 2.7% in the urine	66
	animal toxicology	dermal LD_{50} (rabbits), 4.2 g/kg; oral LD_{50} (rats), 0.79-4.36 g/kg short-term oral: 6.9% n-butyl alcohol and 25% sucrose given in drinking water for 3 wks produced some changes in hepatic mitochondria inhalation: results in irritation of the mucous membranes, intoxication, restlessness, ataxia, prostration, and narcosis; high concentrations can be fatal	
	dermal irritation/sensitization	no data	
	mucosal irritation	15% n-butyl alcohol produced an ocular irritation score of <5/20 and a 40% solution produced a score of >5/20 in rabbit eyes	
	repro/developmental toxicity	fetotoxicity has been demonstrated at maternally toxic levels (1000 mg/kg); no significant behavioral or neurochemical effects were seen in offspring following either maternal or paternal exposure to 3000 or 600 ppm	
	Genotoxicity	negative in an Ames test, did not induce sister chromatid exchange 0.1 or (15% aq.) or micronuclei formation, and did not impair chromosome distribution in mitosis	
	Carcinogenicity	no data	
	clinical assessment of safety	a nail color containing 3% n-butyl alcohol was not a significant irritant or sensitizer in HRIPTs, and this product was not a phototoxin or photoallergen; negative for non-immunological urticaria occupational exposure: n-butyl alcohol (alone or with other solvents) produced complaints of ocular irritation, headache and vertigo, slight irritation of the nose and throat, and dermatitis of the hands and fingers at air concentrations of >50 ppm	
	important Discussion items	uses in products other than nail products are at very low concentrations, so there were no toxicity concerns	
	Conclusion	**safe as used**	
Cetearyl Alcohol	animal toxicology	no data	67
	dermal irritation/sensitization	formulation w/3%, mildly irritating (rabbits)	
	mucosal irritation	formulation w/3%, not irritating	
	repro/developmental toxicity	no data	
	Genotoxicity	no data	
	Carcinogenicity	no data	
	clinical assessment of safety	formulation w/3%: not a sensitizer	
	important Discussion items	no relevant items identified	
	Conclusion	**safe as used**	
Cetyl Alcohol	ADME	in general, long-chain aliphatic alcohols, such as cetyl alcohol, are oxidized to their corresponding fatty acids in mammalian tissues; in rats administered radioactive cetyl alcohol by either stomach tube or thoracic duct fistulas, most of the radioactivity was found in the thoracic duct lymph, indicating good absorption; some of the cetyl alcohol was eliminated unchanged in waste products, but most of the cetyl alcohol was oxidized to palmitic acid and incorporated into triglycerides and phospholipids	67
	animal toxicology	oral LD_{50}(rats): >8.2 g/kg; formulations w/≤4%, no toxic effects; dermal LD_{50}: >2.6 g/kg; formulation w/5%, 2 g/kg; inhalation: 6-h exposure, 26 ppm (rats, mice, guinea pigs), slight irritation of mucous membranes, but no signs of systemic toxicity or mortality; 6 h exposure, 2220 mg/m^3, 100% mortality short-term dermal: 20 day, 11.5%, 5x/day, exfoliative dermatitis, parakeratosis, hyperkeratosis (rabbits); 30 day, 30% in methyl alcohol and propylene glycol, dermal infiltrates of histocytes 3 mos dermal study: formulations w/20%, well-defined erythema, mild edema, no systemic toxicity (rabbits)	
	dermal irritation/sensitization	undiluted, minimally to slightly irritating; formulations w/2-4%, no to well-defined erythema and edema	
	mucosal irritation	formulations w/≤6.36%, mostly non-irritating	
	mucosal irritation	2%: not irritating to genital mucosa of rabbits	
	repro/developmental toxicity	no data	
	Genotoxicity	negative, Ames test	
	Carcinogenicity	no data	
	clinical assessment of safety	100%: not irritating; formulations w/2-11.5%,:at most, mild irritants formulations w/1-8.4%, not sensitizers 30%: 11.2% of eczema patients (pop. 330) had allergic reactions formulations w/1-4%, not photosensitizers	
	important Discussion items	no relevant items identified	
	Conclusion	**safe as used**	

Table 6. Summaries of information on fatty alcohols from previous CIR reports

Ingredient	Parameter Evaluated	Outcome	Reference
Coconut Alcohol	animal toxicology	no data	68
	dermal irritation/sensitization	no data	
	mucosal irritation	no data	
	repro/developmental toxicity	no data	
	Genotoxicity	no data	
	Carcinogenicity	no data	
	clinical assessment of safety	no data	
	important Discussion items	toxicity and use profiles expected to be similar to coconut oil, coconut acid, hydrogenated coconut oil, hydrogenated coconut acid; addressed use in inhalation products; possible issues with botanicals	
	Conclusion	**safe as used**	
Isostearyl Alcohol	animal toxicology	oral LD_{50}: >20 g/kg (rats); formulations w/25-27%, >15 g/kg	67
	dermal irritation/sensitization	formulation w/5%: mild irritant (rabbits); formulation w/25-27%: barely perceptible erythema 0.2-5%: not a sensitizer	
	mucosal irritation	formulations w/5 and 10%, transient irritation; formulations w/25-27%, minimal to mild irritation	
	repro/developmental toxicity	no data	
	Genotoxicity	no data	
	Carcinogenicity	no data	
	clinical assessment of safety	100%: not irritating; formulations w/25-28%, not irritating; deodorant formulation w/ 5%, severe irritation in a 21-day cumulative study 25% in 95% isopropyl alcohol: not a sensitizer; formulations w/5%: sensitization reactions occurred	
	important Discussion items	no relevant items identified	
	Conclusion	**safe as used**	
Myristyl Alcohol	animal toxicology	oral LD_{50} (rats): >8 g/kg; formulation w/0.8%, >5 g/kg; dermal LD_{50}: formulation w/0.8%, >2 g/kg inhalation: 3%, 1 h, ataxia and moderate nasal irritation in all animals 10 min after exposure, no mortality	67
	dermal irritation/sensitization	formulation w/0.8%, non-irritating (rabbits)	
	mucosal irritation	formulation w/0.8%: not irritating; formulation w/3%: mildly irritating (rinsed eyes), moderately irritating (unrinsed eyes)	
	repro/developmental toxicity	no data	
	Genotoxicity	no data	
	Carcinogenicity	no data	
	clinical assessment of safety	formulations w/0.1-0.25%, not irritants; formulations w/0.25-0.8%, not irritating in a 4-wk clinical study formulations w/0.1-0.25%, not sensitizers formulation w/0.1%, not a photosensitizer	
	important Discussion items	no relevant items identified	
	Conclusion	**safe as used**	
Octyl Dodecanol	animal toxicology	oral LD_{50} (rats): >5 g/kg, undiluted; formulation w/10.2%, >25 g/kg; dermal LD_{50}: >3 g/kg	69
	dermal irritation/sensitization	100%: irritation score of 0-1.13/4 (rabbits); 30%: irritation score 0/4 (rabbits); formulations w/4 and 10.2%, mild irritation, at most; technical grade: moderate to severe irritation (rabbits, guinea pigs, rats), no irritation (swine, humans)	
	mucosal irritation	100%: irritation score of 1 or 4/110 (24 h)	
	repro/developmental toxicity	no data	
	Genotoxicity	no data	
	Carcinogenicity	no data	
	clinical assessment of safety	100%: mild irritation in 1/40 subjects; undiluted technical grade: no irritation; formulations w/3-10.2%: essentially non-irritating screening patch tests for contact sensitization in large populations: incidence rate of 0.36% (6/1664) formulation w/10.2%: not phototoxic or photoallergenic	
	important Discussion items	no Discussion	
	Conclusion	**safe as used**	

Table 6. Summaries of information on fatty alcohols from previous CIR reports

Ingredient	Parameter Evaluated	Outcome	Reference
Stearyl Alcohol	ADME	found naturally in various mammalian tissues; readily converted to stearic acid, another common constituent of mammalian tissues; results from several studies indicate that stearyl alcohol is poorly absorbed from the GI tract	69
	animal toxicology	oral LD_{50}: >8 g/kg;	
		3 mos dermal study: formulations w/8%,some dermal effects, , no systemic toxicity (rabbits)	
	dermal irritation/sensitization	100%: minimal to mild primary skin irritant (rabbits)	
		formulation w/24%: not a sensitizer	
	mucosal irritation	100%: mildly irritating	
	repro/developmental toxicity	no data	
	Genotoxicity	negative: Ames test	
	Carcinogenicity	did not promote tumor formation in mice when tested with dimethylbenz[a]anthracene	
	clinical assessment of safety	100%: produced mild irritation in 1/80 subjects; formulations w/14-24% were non- to slightly irritating	
		formulations w/14-2%, not sensitizers	
		screening patch tests for contact sensitization in large population: incidence rate of 0.51% (19/3740)	
	important Discussion items	Discussion not included in report	
	Conclusion	**safe as used**	

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