Safety Assessment of *Hamamelis virginiana* (Witch Hazel)-Derived Ingredients as Used in Cosmetics

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ABSTRACT

The Cosmetic Ingredient Review (CIR) Expert Panel (Panel) assessed the safety of 8 *Hamamelis virginiana* (witch hazel)-derived ingredients as used in cosmetics. Many of these ingredients are reported to function as astringents and skin-conditioning agents - miscellaneous in cosmetics. The Panel reviewed the data relevant to the safety of these ingredients. Because final product formulations may contain multiple botanicals, each containing the same constituents of concern, formulators are advised to be aware of these constituents and to avoid reaching levels that may be hazardous to consumers. Industry should continue to use good manufacturing practices to limit impurities. The Panel concluded that these *Hamamelis virginiana* (witch hazel)-derived ingredients are safe in cosmetics in the present practices of use and concentration described in this safety assessment when formulated to be non-irritating and non-sensitizing.

INTRODUCTION

The Panel assessed the safety of 8 *Hamamelis virginiana* (witch hazel)-derived ingredients as used in cosmetics.

Hamamelis Virginiana (Witch Hazel) Bark/Leaf Extract	Hamamelis Virginiana (Witch Hazel) Flower Water
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract	Hamamelis Virginiana (Witch Hazel) Leaf Extract
Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract	Hamamelis Virginiana (Witch Hazel) Leaf Water
Hamamelis Virginiana (Witch Hazel) Extract	Hamamelis Virginiana (Witch Hazel) Water

According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI *Dictionary*), many of these ingredients are reported to function as an astringent and skin-conditioning agent – miscellaneous in cosmetics (Table 1).[1] However, the only stated function therein for Hamamelis Virginiana (Witch Hazel) Flower Water is fragrance ingredient.

To avoid redundancy of effort, CIR may exclude from review ingredients that are known to exclusively function as fragrance ingredients (such as Hamamelis Virginiana (Witch Hazel) Flower Water) when the ingredient has been, or will be, evaluated by the Research Institute for Fragrance Materials (RIFM). However, because communications with RIFM in November 2017 revealed that this ingredient has neither been assessed for safety by the RIFM Expert Panel, nor is this ingredient on RIFM's prioritized agenda to be reviewed in the foreseeable future, this ingredient is not excluded from this CIR review.

Drug astringent – skin protectant drug is also listed as a function of Hamamelis Virginiana (Witch Hazel) Water. Drug astringent is not a cosmetic function, and therefore use in that manner is not being assessed in this report.

The names of the ingredients in this report are written in accordance with International Nomenclature Cosmetic Ingredient (INCI) naming conventions, i.e., capitalized without italics and without abbreviations. When referring to the plant from which these ingredients are derived, the standard taxonomic practice of using *italics* will be followed (e.g., *Hamamelis virginiana*).

Often in the published literature, the information provided is not sufficient to determine how well the tested substance represents the cosmetic ingredient (e.g., "hamamelis water" with the CAS number 68916-39-2). In such cases, the INCI naming conventions are not used, unless it is clear that the test substance is similar to a cosmetic ingredient.

Botanicals, such as *Hamamelis virginiana* (witch hazel)-derived ingredients, may contain hundreds of constituents, some of which may have the potential to cause toxic effects. For example, geraniol and linalool are constituents of the *Hamamelis virginiana* (witch hazel) plant; geraniol is a potential dermal sensitizer, as are the oxidation products of linalool.[2-4] In this assessment, CIR is reviewing the potential toxicity of each of the *Hamamelis virginiana* (witch hazel)-derived ingredients as a whole, complex mixture. CIR is not reviewing the potential toxicity of the individual constituents herein.

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an exhaustive search of the world's literature. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that CIR typically evaluates, is provided on the CIR website (http://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; http://www.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

Pertinent data were discovered in other reports, including reports by the Committee on Herbal Medicinal Products (HMPC), the World Health Organization (WHO), and the European Agency for the Evaluation of Medicinal Products (EMEA), Veterinary Medicines Evaluation Unit.[5-7] Reports by these organizations are cited in this assessment to identify the source of the data obtained from these summaries.

CHEMISTRY

Definition

The definitions of the ingredients in this safety assessment are provided in Table 1.

All of these ingredients comprise mixtures of substances derived from the botanical source, *Hamamelis virginiana*, which is commonly called witch hazel.

Plant Identification

Hamamelis virginiana, a member of the family Hamadelidaceae, is indigenous to damp woods on the Atlantic coast of North America, regionally from Florida to Nova Scotia, and may be found as far west as Texas.[5,7-10] The appearance/ structure of the plant and leaves vary widely with no consistent pattern of variation or geographic correlation. The plant may be a tall shrub with the branches coming from the base or small tree of up to 4.6 m tall. The leaves are 1 to 5 cm long and may alternate or stipulate, have short petioles, and may be unequilateral or rhomboid-ovate, with an oblique base and sinuate or sinuate-dentate margin. The flowers are golden-yellow and thread-like, and grow in axillary clusters (Figure 1).

Hamamelis virginiana likely reproduces through insect pollination instead of wind pollination.[5,7-10] The leaves fall in autumn about the same time as fruits ripen from the flowers of the previous year. The fruit are a 2-beaked, 2-celled, woody capsules each cell containing a single black seed. This plant is unusual in that it has flowers and fruit at the same time.

Physical and Chemical Properties

Physical and chemical properties of Hamamelis Virginiana (Witch Hazel) Leaf Water (at 85% to 86%) and Hamamelis Virginiana (Witch Hazel) Water (at 85% to 86%) in grain alcohol or ethanol are presented in Table 2.

Method of Manufacture

The definitions of several of the *Hamamelis virginiana* (witch hazel)-derived ingredients in this safety assessment give insight into possible methods of manufacture. For example, the definition for Hamamelis Virginiana (Witch Hazel) Flower Water states that this ingredient is an aqueous solution of the steam distillates obtained from the flowers of *Hamamelis virginiana*.[1]

Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract

A manufacturer reported that the method of manufacture for a product mixture containing Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract (10%) starts with the testing of the collected *Hamamelis virginiana* plant material.[11] If the materials pass (criteria not specified), the plant matter is mechanically cleaned to remove unnecessary material. The twigs, bark, and leaves are then processed by grinding and milling. An aqueous extraction is performed at a specific pH and temperature for a specified duration (not provided). Phenoxyethanol, tetrasodium ethylenediaminetetraacetic acid (EDTA), methylparaben, ethylparaben, butylparaben, propylparaben, and isobutylparaben are added to the extract (to make a trade name mixure). The trade name mixture is filtered and the batch is sampled for quality control. Adjustments are made if needed. After the extract is packaged, it is sampled for microbes.

A similar method of manufacture was reported for a product mixture containing Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract (20%).[11] The only difference is that the propylene glycol is added to dilute the mixture after the aqueous extraction is performed, and the EDTA is not added to the trade name mixture.

Hamamelis Virginiana (Witch Hazel) Extract

A manufacturer reported that the method of manufacture for a product mixture containing Hamamelis Virginiana (Witch Hazel) Extract (5%) starts with grinding and milling the collected *Hamamelis virginiana* plants.[12] The resulting material is extracted with cyclopentasiloxane at a specific pH and temperature for a specified duration (not provided). The extract is filtered and the batch is sampled for quality control. Adjustments are made if needed. After the extract is packaged, it is sampled for microbes.

Hamamelis Virginiana (Witch Hazel) Leaf Water

A manufacturer reported that a trade name mixture composed of Hamamelis Virginiana (Witch Hazel) Leaf Water and alcohol is a distillate prepared from recently harvested and partially dried leaves of *Hamamelis virginiana*, containing natural oils, and 14% alcohol.[13]

Hamamelis Virginiana (Witch Hazel) Water

A manufacturer reports that a trade name mixture composed of Hamamelis Virginiana (Witch Hazel) Water and alcohol is a distillate prepared from recently cut and partially dried dormant twigs of *Hamamelis virginiana*, containing natural oils, and 14% alcohol.[14]

Composition and Impurities

The method of manufacture significantly impacts the compositions of *Hamamelis virginiana* (witch hazel)-derived ingredients. For example, distilled ingredients have fewer astringent tannins than a water extract.[15]

Hamamelis virginiana (Witch Hazel) Plant (Source Material)

Polyphenols - The leaves contain up to, but not more than, 3% tannins.[7,16] The cortex/bark of the stems contains up to 12%, but not less than 4%, tannins. Both hydrolysable and condensed tannins are present, with the latter predominating.[7]

Leaf tannins are a mixture of gallic acid (10%), hydrolyzable hamamelitannin (1.5%) and condensed proanthocyanidins (88.5%). Bark tannins are similar qualitatively, but have a much greater hamamelitannin concentration (up to 65% of a hydroalcoholic extract). Polyphenols, other than tannins, include phenolic acids and flavonoids. At least 27 phenolic constituents have been identified.

Flavonoids – The leaves contain flavonoid galactosides and glucuronides and other flavonoids such as kaempferol, quercetin, quercitrin, and isoquercitrin.[5]

Catechins - Catechins include (+)-catechin, (+)-gallocatechin, (-)-epicatechin gallate(III), and (-)-epigallocatechin gallate(III). Oligomeric procyanidins are also present. [7,16]

Volatile oil – Both bark and leaves contain volatile oil (0.1% and 0.01% to 0.05%, respectively).[6] The composition of the volatile fraction obtained by water distillation from the leaves and bark of *Hamamelis virginiana*, determined by gas chromatography-mass spectrometry (GC-MS), consists of approximately 175 identified compounds in the leaves and 168 compounds in the bark.[2,5] The dominating substances were represented by a homologous series of alkanes, alkenes, aliphatic alcohols, related aldehydes, ketones, and fatty acid esters. The volatile oil contains hexane-2-ol, hexenol, α- and β-ionones, eugenol, safrole (maximum 0.2% of the volatile oil) and sesquiterpenes. Other constituents include gallic acid. The bark contains significantly higher levels of phenylpropanoids and sesquiterpenoids in the volatile fractions compared to the leaves, which contain higher amounts of monoterpenoids.[5] Other components include kaempferol, quercetin, chlorogenic acid isomers, and hydroxycinnamic acids.[7] The volatile oil contains small amounts of safrole and eugenol as well as numerous other minor components, such as resin, wax, and choline.

The constituents in the volatile fraction of water-distilled (4 h) leaves and bark from freshly harvested *Hamamelis virginiana* using *n*-hexane as the collector solvent are listed in Table 3.[2] The constituents were identified by GC-MS.

During harvest, *Hamamelis virginiana* plants can be confused with *Coryllus avellana* (hazelnut); this may be a source of impurities.[5] The two plants can be distinguished by anatomical and analytical examination.

Constituents of Concern – Table 4 lists constituents of concern of *Hamamelis virginiana* plants. These plants are reported to contain linalool and quercetin.[2,17] Safrole was also found at a level of < 0.2% in *Hamamelis virginiana* leaf oil.[5] Possible contaminants (e.g., tributylphosphate and dibutyl phthalate) from the volatile fraction of water-distilled leaves and bark are noted in Table 3.

The International Fragrance Association (IFRA) publishes restrictions for fragrance ingredients. Constituents of *Hamamelis virginiana* that have restrictions established by the IFRA Standards are listed in Table 5.[18]

Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract

One manufacturer reported that Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract is supplied in product mixtures.[19-22] Two product mixtures that include Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract at 10.00% or 20.00%, also contain tetrasodium EDTA (0.1%) or propylene glycol (48%), respectively (Table 6). Both of these product mixtures also contain paraben ingredients (0.138%). These product mixtures were certified to not include detectable allergens including amyl cinnamal, citral, coumarin, eugenol, geraniol, and linalool (Table 7). These product mixtures are also certified to not include detectable pesticides including alachlor, diazinon, heptachlor, dichlorodiphenyltrichloroethane (DDT), and parathion. These two product mixtures are also specified to contain < 20 ppm heavy metal, < 10 ppm lead, < 2 ppm arsenic, and < 1 ppm cadmium.[23,24] Microbial content is < 100 colony forming units (CFU)/g with no pathogens, < 100 CFU/g yeast and mold, and 0 CFU/g gram-negative bacteria.

Hamamelis Virginiana (Witch Hazel) Extract

One manufacturer reported that Hamamelis Virginiana (Witch Hazel) Extract is supplied as a product mixture of 5.00% Hamamelis Virginiana (Witch Hazel) Extract and 95.00% cyclopentasiloxane.[25,26] This product mixture was certified to not include detectable allergens including amyl cinnamal, citral, coumarin, eugenol, geraniol, and linalool (Table 7). This product mixture was also certified to not include detectable pesticides including alachlor, diazinon, heptachlor, DDT, and parathion. This product mixture is also specified to contain < 20 ppm heavy metal, < 10 ppm lead, < 2 ppm arsenic, and < 1 ppm cadmium.[27] Microbial content is < 100 CFU/g with no pathogens, < 100 CFU/g yeast and mold, and 0 CFU/g gram-negative bacteria.

Hamamelis Virginiana (Witch Hazel) Leaf Water

A manufacturer reports that Hamamelis Virginiana (Witch Hazel) Leaf Water is supplied as a trade name mixture at 85% to 86% of the ingredient with 14% to 15% ethanol.[28]

Specifications for a trade name mixture containing Hamamelis Virginiana (Witch Hazel) Leaf Water and 14% grain alcohol state it is to contain < 50 mg/100 mL nonvolatile residue, < 10 CFU/mL yeast and mold, a maximum of 1 CFU/mL gram-negative bacteria, and is below the levels of detection for acetone, other ketones, isopropyl alcohol, and *t*-butyl alcohol.[13]

The United States Pharmacopeia and National Formulary has announced its intention to revise the witch hazel monograph.[29] Data showed that the distillation process reduces the risk of pesticides present in the official article. Therefore, because the official article is not a plant material but a distillate, testing for pesticides may not add value in the monitoring of the quality of witch hazel. The current specifications for nonvolatile residue is not to exceed 25 mg/100 ml (0.025%).[14,30]

Hamamelis Virginiana (Witch Hazel) Water

Hamamelis Virginiana (Witch Hazel) Water is reported by a manufacturer to be supplied as a trade name mixture at 85% to 86% of the ingredient with 14% to 15% grain alcohol or ethanol.[31-33]

Specifications for Hamamelis Virginiana (Witch Hazel) Water and 14% grain alcohol state it is to contain < 25 mg/100 mL nonvolatile residue, < 10 CFU/mL yeast and mold, a maximum of 1 CFU/mL bacteria, and is below the levels of detection for acetone, other ketones, isopropyl alcohol, and t-butyl alcohol, and formaldehyde.[14,30,34] Tannins are limited to < 0.03 mg/mL.

UV Absorption

Hamamelis virginiana (Witch Hazel) Plant (Source Material)

In ethanol extracts of dried *Hamamelis virginiana* plant material (most likely leaves), the light absorbance curves peaked between 250 and 280 nm, depending on the method of extraction.[35] Extracts were prepared by reperculation and microwave assisted extraction, and tested at 3%, 10%, and 40%.

USE

Cosmetic

The safety of the cosmetic ingredients included in this assessment is evaluated based on data received from the U.S. Food and Drug Administration (FDA) and the cosmetic industry on the expected use of these ingredients in cosmetics. Use frequencies of individual ingredients in cosmetics are collected from manufacturers and reported by cosmetic product category in FDA's Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by the cosmetic industry in response to surveys, conducted by the Personal Care Products Council (Council), of maximum reported use concentration by product category.

According to VCRP survey data received in 2018, Hamamelis Virginiana (Witch Hazel) Extract is reported to be used in 393 formulations (305 in leave-on formulations, 86 in rinse-off formulations, and 2 in formulations that are diluted for the bath; Table 8).[36] Hamamelis Virginiana (Witch Hazel) Water is reported to be used in 376 formulations (244 in leave-on formulations, 122 in rinse-off formulations, and 10 in formulations that are diluted for the bath) and Hamamelis Virginiana (Witch Hazel) Leaf Extract is reported to be used in 218 formulations (143 in leave-on formulations, 68 in rinse-off formulations, and 7 in formulations that are diluted for the bath). All other in-use ingredients are reported to be used in 125 or fewer formulations. The VCRP has an entry for a single use for "Hamamelis Virginiana (Witch Hazel) Bark Extract" and 38 uses reported for "Witch Hazel". These are not INCI names in the wINCI *Dictionary*, but are included to provide complete information.

The results of the concentration of use survey conducted by the Council in 2017 indicate Hamamelis Virginiana (Witch Hazel) Water has the highest reported maximum concentration of use; it is used at up to 43% (in the category of other skin care preparations).[37] All other in-use ingredients are reported to be used at up to 4.3% or less.

In some cases, reports of uses were received in the VCRP, but concentration of use data were not provided. For example, Hamamelis Virginiana (Witch Hazel) Flower Water is reported to be used in 39 cosmetic formulations, but no use concentration data were reported. In other cases, no uses were reported in the VCRP, but concentration of use data were received from industry. Hamamelis Virginiana (Witch Hazel) Leaf Water had no reported uses in the VCRP, but use concentrations in paste masks and mud packs were provided in the industry survey. It should be presumed there is at least one use in every category for which a concentration is reported.

There were no uses reported to the VCRP and no concentration of use reported in response to the industry survey for Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Extract and Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract.

Several of these ingredients were reported to be used in formulations used near the eyes (up to 30.6% Hamamelis Virginiana (Witch Hazel) Water in eye lotions and other eye makeup preparations), and in formulations that may come in contact with mucous membranes and possibly ingested (including lipsticks, mouthwashes, and breath fresheners; highest reported concentration at up to 30.6% Hamamelis Virginiana (Witch Hazel) Water in lipsticks). Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract is reported to be used in a baby shampoo, but no concentrations of use were reported.

Additionally, some of the *Hamamelis virginiana* (witch hazel)-derived ingredients are used in cosmetic sprays and could possibly be inhaled; for example, Hamamelis Virginiana (Witch Hazel) Water is used in body and hand spray formulations at up to 25.8%. 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.[38,39] 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., they would not enter the lungs) to any appreciable amount.[40,41] Hamamelis Virginiana (Witch Hazel) Water was reported to be used in face powders at concentrations up to 0.093%. Conservative estimates of inhalation exposures to respirable particles during the use of loose-powder cosmetic products are 400- to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.[42-44]

Non-Cosmetic

Hamamelis virginiana (witch hazel), under the name "witch hazel" may be used as an active ingredient as an astringent in over-the-counter (OTC) anorectal drug products at 10% to 50% and OTC skin protectant drug products (as an astringent active ingredient with no limit specified). [21CFR346.18; 21CFR347.12] Hamamelis Virginiana (Witch Hazel) Extract is used in an OTC skin astringent at 86%.[37]

Hamamelis virginiana (witch hazel) preparations are commonly used for dermatological conditions, including diaper-related dermatitis; however, clinical studies supporting these uses are generally lacking.[5] In Europe, extracts of *Hamamelis virginiana* (witch hazel) folium and/branches are used in teas/poultices (leaf), liquid and dry extracts (leaf:ethanol at 1:1 or 1:2 with 30% to 60% ethanol; bark:ethanol at 5:1 to 7:1 with 30% ethanol, respectively), distillates (leaf/branches:ethanol at 1:1.12 to 1:2.08 with ethanol), ointments, creams, tinctures (leaf/branches:ethanol at 1:10 with 45% ethanol), suppositories, and liquid extracts to treat hemorrhoids, fever, nose and gum bleeds, lesions, varicose veins, and other minor inflammations of the skin and mucosa. *Hamamelis virginiana* (witch hazel) folium is also used to make eye drops (10%) to treat irritation.

Hamamelis virginiana (witch hazel), 2.5% to 10.8% (w/w) of an extract of the leaves, is used in veterinary medicine as a topical solution, or as an ointment, combined with other herbal extracts, to promote wound-healing of minor injuries to the skin, treatment of skin inflammations, ulcerations, and dermatoses.[6]

TOXICOKINETIC STUDIES

Dermal Penetration

Obtaining data on the toxicokinetics of *Hamamelis virginiana* (witch hazel)-derived ingredients would not be practical because these ingredients are complex mixtures. However, a manufacturer reported that *Hamamelis virginiana* (witch hazel) extracts dermally applied in therapeutic amounts do not penetrate into the deeper layers of the skin because of the astringency of their ingredients; thus, they appear to be minimally absorbed into the blood circulation.[5]

Absorption, Distribution, Metabolism, and Excretion (ADME)

No published ADME studies were discovered and no unpublished data were submitted.

TOXICOLOGICAL STUDIES

Acute Dose Toxicity

No published acute dermal or inhalation toxicity studies were discovered and no unpublished data were submitted.

Oral

The oral administration of a single dose of a *Hamamelis virginiana* (witch hazel) preparation (10 to 20 g; preparation was not specified) showed no toxic effect in mice and rats.[5] No further details were provided.

Anorectal

New Zealand White rabbits (n = 2/sex) were administered suppositories containing *Hamamelis virginiana* (witch hazel) ethanol extract (0, 20, 100, or 300 mg/kg).[45] The extract was characterized as having a minimum of 10% tannins and containing gallic acid. The suppository was comprised of hard fat, white beeswax, and colloidal anhydrous silica. The suppositories were melted and a single dose was administered with a graduated pipette with a plastic tip. The rabbits were observed for 7 h after dosing and then daily for 2 weeks. A local examination of the anorectal region was conducted on days 2, 7 and 14 post-dosing. Blood was sampled on the last day of the observation period. No rabbits died as the result of the experiment. There were no differences in body weights among test groups. There were no changes in liver and kidney functions. There was a non-dose-dependent increase in serum urea content in all treatment rabbits. There were no hematological effects observed. The no-observed-adverse-effects level (NOAEL) was > 300 mg/kg.

Short-Term Toxicity Studies

No published short-term oral, dermal, or inhalation toxicity studies were discovered and no unpublished data were submitted.

Anorectal

Sprague Dawley rats (n = 5/sex) were administered suppositories containing *Hamamelis virginiana* (witch hazel) ethanol extract (0, 20, 100, or 300 mg/kg/day) for 28 days.[45] The suppositories were melted and administered with a graduated pipette with a plastic tip. The rats were observed for 1 h after dosing, and then observed and weighed daily. Feed and water consumption were assessed weekly. Blood was sampled by cardiac puncture on the last day of the observation period. The rats were killed and necropsied; the digestive tract was included in the examinations. The liver, kidney, and rectal biopsies were isolated from two rats/sex in the placebo and high-dose groups; these samples were fixed in formaldehyde and examined under light microscope. No rats died as a result of the experiment and no clinical signs were observed. There were no differences in body weight gains among test groups. The observed organs (liver, kidneys, spleen,

submandibular salivary glands, heart, testis, and lungs) were similar among placebo and treatment groups. There were no changes in liver and kidney functions without changes in serum lipids and protein profiles. There were no hematological effects observed. The NOAEL was > 300 mg/kg/day.

Subchronic

No published dermal or inhalation subchronic toxicity studies were discovered and no unpublished data were submitted.

Oral

Hamamelis virginiana (witch hazel; preparation not specified) at 100 mg/kg/day was orally administered to rats for three months. There were no abnormalities reported. No further information was available.[5]

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY (DART) STUDIES

No published developmental or reproductive toxicity studies were discovered and no unpublished data were submitted.

GENOTOXICITY STUDIES

In Vitro

Genotoxicity studies are summarized in Table 9.

An Ames assay of a product containing Hamamelis Virginiana Leaf Extract (6%; tested at up to 3100 µg/plate Hamamelis Virginiana Leaf Extract) was negative.[46] Hamamelis Virginiana (Witch Hazel) Water (concentration not specified) was not genotoxic in a *Salmonella* mammalian microsome assay, with and without metabolic activation.[5] A sister chromatid exchange (SCE) assay and a chromosome aberration test were performed on Hamamelis Virginiana (Witch Hazel) Water at up to 5000 µg/mL, with negative results.[47] Hamamelis Virginiana (Witch Hazel) Water (up to 5000 µg/mL) was tested for mutagenic potential in the L5178Y tk+/- mouse lymphoma cell forward mutation assay, with and without metabolic activation, and was not identified as a mutagen.[5,48]

Hamamelis virginiana (witch hazel) leaf oil (under the CAS number 68916-39-2; 100 to 10,000 µg/plate) was not genotoxic in an Ames assay using *Salmonella typhimurium* (strains TA98, TA100, TA1535, and TA1537), with and without metabolic activation.[49]

In Vivo

No published in vivo genotoxicity studies were discovered and no unpublished data were submitted.

CARCINOGENICITY STUDIES

Dermal

In a skin painting study, a *Hamamelis virginiana* (witch hazel)-derived substance (50% in deionized water and at 100%; under the name "Hamamelis water" with the CAS number 68916-39-2) was dermally administered to male and female F344 rats and $B6C3F_1$ mice, 5 days per week for 2 years, in a National Toxicology Program (NTP) experiment.[50-52] There was a trend for increased tumors, fibromas, or fibrosarcomas noted in the male rats and alveolar/bronchiolar adenomas or carcinomas in female mice, but none of these observations were statistically-significant. There were no other signs of carcinogenicity in either species at either concentration. No further details were provided. A technical report number was assigned to the chronic study of this test article. It was not clear why no technical report was prepared.

Subcutaneous

An aqueous *Hamamelis virginiana* (witch hazel) leaf extract (10 mg in saline; 0.5 mL) was subcutaneously injected into the flanks of NIH black rats (n = 15/sex) once per week for up to 78 weeks.[53] Saline was the control. The extract was made from collected wild leaves that were powdered and extracted with hot water, and lyophilized. The dose was based on preliminary studies to find the amount of plant material that did not produce any systemic toxicity or local necrosis and sloughing (this dose did cause some swelling, which disappeared within 1 to 2 weeks). Injections were conducted for 78 weeks or until a tumor was detected. The detected tumor was allowed to grow to sufficient size, and then the rat was killed and necropsied. Rats that lived through treatment were observed for an additional 12-week period, and then they were killed and necropsied. Tumor tissue and organs (including regional lymph nodes, lungs, liver, spleen, and kidneys) were examined. No tumors were detected in the control group. Three males in the treatment group had tumors that were discovered in weeks 72 to 73. No tumors were observed in the female rats. Two males (weeks 24 and 57) and one female (week 59) died of lung infections. The number of treated rats with tumors was not significantly greater than that of the controls.

OTHER RELEVANT STUDIES

Comedogenicity

A 4-week use study was conducted of a sunless tanner that contained Hamamelis Virginiana (Witch Hazel) Water (6.02%).[54] Female subjects (n = 19) were examined before and after the test period for comedogenicity/clogged pores. The test material did not increase the number of acnegenic lesions over the test period.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Irritation

In Vitro

EpiDerm™ assays of two product mixtures that contain Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract (5% and 10%) were negative. [55,56] In an EpiDerm™ assay of Hamamelis Virginiana (Witch Hazel) Extract (5% in cyclopentasiloxane), irritation potential was predicted to be negative.[57]

Human

A patch test of a face product containing Hamamelis Virginiana (Witch Hazel) Water (8.5%; 25 µL) was conducted.[58] The test substance was applied to the scapular area of subjects (n = 11) under occlusion using Finn chambers for 48 h. The test sites were observed at 30 min and 24 h after removal. The test substance was found to be a nonirritant.

As described in the Comedogenicity section, a 4-week use study was conducted of a sunless tanner that contained Hamamelis Virginiana (Witch Hazel) Water (6.02%).[54] Female subjects (n = 19) were examined before and after the test period for erythema, edema, and dryness as well as non-inflammatory and inflammatory lesions. One subject reported "tingling" for 5 min after application on the last two days of the test. There were no signs of irritation with dermal examination.

Sensitization

Human repeat insult patch tests (HRIPTs) are presented in Table 10.

Hamamelis Virginiana (Witch Hazel) Leaf Extract and Hamamelis Virginiana (Witch Hazel) Water were not irritating or sensitizing in HRIPTs at up to 0.45% and 25.80%, respectively. [46,59-61]

Photosensitization/Phototoxicity

In Vitro

An *in vitro* phototoxicity assay of a trade name mixture that contains Hamamelis Virginiana (Witch Hazel) Leaf Extract (6%) was conducted.[46] The test substance (up to 17,000 µg/mL; 1020 µg/mL Hamamelis Virginiana (Witch Hazel) Leaf Extract) was administered to Balb/c 3T3 cells with and without a UVA dose of 5 J/cm^2. No cytotoxicity was observed at any concentration tested with or without UVA irradiation indicating no phototoxicity.

OCULAR IRRITATION STUDIES

In Vitro

EpiOcular™ assays of two product mixtures that contain Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract (5% and 10%) were negative for predicting ocular irritation potential.[55,56] In an EpiOcular™ assay of Hamamelis Virginiana (Witch Hazel) Extract (5% in cyclopentasiloxane), irritation potential was predicted to be negative.

Human

A 4-week use study was conducted of a sunless tanner that contained Hamamelis Virginiana (Witch Hazel) Water (6.02%).[54] Female subjects (n = 10 that did not wear contact lenses, 9 that wore contact lenses) were examined before and after the test period by an ophthalmologist for lacrimation, eyelid integrity, palpebral and bulbar conjunctival irritation, corneal tissue involvement, and changes in contact lenses. Subjective responses for signs of ocular irritation, such as stinging, burning, itching, dryness, and foreign body sensation, were also noted during the study. Trace increases in redness of the palpebral conjunctivae that were observed in one subject were deemed not related to the test material. There were no other differences in the eye examinations before and after the use period.

CLINICAL STUDIES

Multicenter Studies

In a multicenter, prospective pediatric cohort study, subjects of different age groups (27 days to 1 year; 1 to 5 years; 6 to 11 years of age) suffering from superficial skin lesions, diaper skin rash, or other local inflammations of skin and mucous membranes were treated in a randomized manner with either an ointment containing *Hamamelis virginiana* (witch hazel; concentration, composition, and source not specified; n = 231) or dexpanthenol (control n = 78).[5,62] The recommended individual observation periods were 7 to 10 days; dosage was based on the recommendations of the treating physician. Tolerability of the ointment containing *Hamamelis virginiana* (witch hazel) was assessed as excellent or good by 99.1% of the doctors and 98.2% of the parents (dexpanthenol: 97.4% and 92.3%, respectively). Two adverse events that were

potentially *Hamamelis virginiana* (witch hazel)-related (i.e. erythema and burning sensation) resolved by the end of the treatment period.

Cross-Allergenicity

Subjects (n = 12) that were confirmed to be sensitized to chamomile (thus, Compositae-sensitive) were administered patch tests for other plant-derived extracts, including an aqueous-alcoholic *Hamamelis virginiana* (witch hazel) distillate (concentration and method of extraction not specified).[63] One subject had a positive reaction the *Hamamelis virginiana* (witch hazel) distillate.

Patients (n = 1032) that were in clinics to be patch tested for allergens were administered additional patch tests for ointments that contain botanical extracts, including *Hamamelis virginiana* (witch hazel) extract (25%).[64] A total of four subjects had positive results to the ointment containing *Hamamelis virginiana* (witch hazel) extract. Two of these subjects also had reactions to other ointments and to "wool fat," which is one of the ingredients in the ointments.

Damaged Skin

Studies on the use of *Hamamelis virginiana* (witch hazel)-derived substances on damaged skin are summarized in Table 11.

There were no reported adverse effects when a cream containing Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract (10%) was applied to skin damaged by UVB light.[65] There were no reported adverse effects from an oil/water (o/w) emulsion containing *Hamamelis virginiana* (witch hazel) distillate (up to 0.00256% *Hamamelis* ketone) applied to skin damaged by UVB light or tape stripping,[66] or from three oil/water (O/W) emulsions containing *Hamamelis virginiana* (witch hazel) distillates (10% *Hamamelis* ketone) from different suppliers applied to skin damaged by UVB light.[67]

There were no adverse events attributed to a cream containing *Hamamelis virginiana* (witch hazel) distillate (up to 0.00064%) when applied to patients with moderately severe atopic eczema for 14 days.[68]

Case Reports

A 31-year-old non-atopic woman started to use a new eye gel that contained "witch hazel distillate," after which edema developed around the eyes within 1 week.[69] At the same time, she was treated with 1% hydrocortisone-17-butyrate for dermatitis of the lower limbs. She stopped using the eye gel, but instead started to use alternative remedies (not specified). Over the following days, edema spread to the rest of the face and neck and then presented as eczema. She was treated systemically with corticosteroid and told not to use any cosmetics or other treatments. The dermatitis resolved and did not relapse. A patch test of the eye cream and its components was conducted. At the readings on day 3, the patch test had positive results for the eye cream (+) and for "witch hazel distillate" in a concentration-dependent manner (1%, -; 5%, +?; 10%, +; 50%, ++; 100%, ++).

SUMMARY

The Panel assessed the safety of 8 *Hamamelis virginiana* (witch hazel)-derived ingredients as used in cosmetics. According to the wINCI *Dictionary*, the cosmetic functions of these ingredients include cosmetic astringent and skin-conditioning agent – miscellaneous.

Hamamelis virginiana (witch hazel), a member of the family Hamadelidaceae, is indigenous to damp woods on the Atlantic coast of North America ranging from Florida to Nova Scotia.

In ethanol extracts of dried *Hamamelis virginiana* (witch hazel) plant material (most likely leaves), the light absorbance curves peaked between 250 and 280 nm, with variations depending on the method of extraction.

According to VCRP survey data received in 2018, Hamamelis Virginiana (Witch Hazel) Extract is reported to be used in 393 formulations (mostly leave-ons), Hamamelis Virginiana (Witch Hazel) Water is reported to be used in 376 formulations, and Hamamelis Virginiana (Witch Hazel) Leaf Extract is reported to be used in 218 formulations. All other in-use ingredients are reported to be used in 125 or fewer formulations. The results of the concentration of use survey conducted by the Council in 2017 indicate Hamamelis Virginiana (Witch Hazel) Water has the highest reported maximum concentration of use; it is used at up to 43% (in the category of other skin care preparations). All other in-use ingredients are reported to be used at up to 4.3% or less.

In the United States, *Hamamelis virginiana* (witch hazel), under the name "witch hazel" may be used as an active ingredient as an astringent in OTC anorectal drug products at 10% to 50% and in OTC skin protectant drug products (no limit specified).

The oral administration of a single dose of a *Hamamelis virginiana* (witch hazel) preparation (10 to 20 g; preparation was not specified) showed no toxic effect in mice and rats. There were no abnormalities reported when *Hamamelis virginiana* (witch hazel) at 100 mg/kg/day was orally administered to rats for 3 months.

In an acute study in rabbits and a 28-day study in rats of suppositories containing a *Hamamelis virginiana* (witch hazel) ethanol extract, there was no mortality, no differences in body weights, no changes in liver and kidney function, and no hematological effects in both studies. The NOAEL was > 300 mg/kg.

Hamamelis Virginiana Leaf Extract and Hamamelis Virginiana (Witch Hazel) Water were not genotoxic in various assays. An Ames assay of a product containing Hamamelis Virginiana Leaf Extract (6%; tested at up to 3100 µg/plate

Hamamelis Virginiana Leaf Extract) was negative. Hamamelis Virginiana (Witch Hazel) Water was not genotoxic in a *Salmonella* mammalian microsome assay, a SCE assay, a chromosome aberration test (up to 5000 µg/mL), and a L5178Y tk+/- mouse lymphoma cell forward mutation assay.

In a skin painting study, a *Hamamelis virginiana* (witch hazel)-derived substance (50% in deionized water and at 100%) was dermally administered to male and female rats and mice for 2 years in a NTP study. There were no significant signs of carcinogenicity in either species at either concentration.

The number of treated rats with tumors was not significantly greater than that of the controls when an aqueous *Hamamelis virginiana* (witch hazel) leaf extract (10 mg in saline) was subcutaneously injected into the flanks of rats once per week for up to 78 weeks.

EpiDerm™ assays of two product mixtures that contain Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract (5% and 10%) predicted that there was no dermal irritation potential. In an EpiDerm™ assay of Hamamelis Virginiana (Witch Hazel) Extract (5%), irritation potential was predicted to be negative.

A face product containing Hamamelis Virginiana (Witch Hazel) Water (8.5%) was found to be a non-irritant in a patch test. There were no signs of dermal irritation from a sunless tanner that contained Hamamelis Virginiana (Witch Hazel) Water (6.02%) in a 4-week use test.

No irritation or sensitization was reported in HRIPTs of Hamamelis Virginiana (Witch Hazel) Leaf Extract at 0.45% and in products containing Hamamelis Virginiana (Witch Hazel) Water at 6.02%, 6.88%, or 25.80%.

EpiOcular™ assays of two product mixtures that contain Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract (5% and 10%) predicted that there was no ocular irritation potential. In an EpiOcular™ assay of Hamamelis Virginiana (Witch Hazel) Extract (5%), irritation potential was predicted to be negative. There were no signs of ocular irritation from a sunless tanner that contained Hamamelis Virginiana (Witch Hazel) Water (6.02%) in a 4-week use test.

In a multicenter, prospective pediatric cohort study, subjects suffering from superficial skin lesions, diaper skin rash, or other local inflammations of skin and mucous membranes were treated with either an ointment containing either *Hamamelis virginiana* (witch hazel; concentration, composition, and source not specified) or dexpanthenol (control). Only two adverse events were potentially related to the *Hamamelis virginiana* (witch hazel; i.e.: erythema and burning sensation), which were resolved by the end of the treatment period.

One of 12 subjects that were confirmed to be sensitized to chamomile (thus, Compositae-sensitive) had a positive reaction to *Hamamelis virginiana* (witch hazel) distillate in a patch test. Four of 1032 patients had positive results to an ointment containing *Hamamelis virginiana* (witch hazel) extract in a patch test.

There were no reported adverse effects when a cream containing Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract (10%) was applied to skin damaged by UVB light.There were no reported adverse effects from an o/w emulsion containing *Hamamelis virginiana* (witch hazel) distillate (up to 0.00256% *Hamamelis* ketone) applied to skin damaged by UVB light or tape stripping. There were no reported adverse effects from o/w emulsions containing *Hamamelis virginiana* (witch hazel) distillates (10% *Hamamelis* ketone) from different suppliers applied to skin damaged by UVB light.

There were no adverse events attributed to a cream containing *Hamamelis virginiana* (witch hazel) distillate (up to 0.00064%) when applied to patients with moderately severe atopic eczema for 14 days.

DISCUSSION

The Panel examined the oral toxicity, genotoxicity, carcinogenicity, dermal irritation, and sensitization studies of *Hamamelis virginiana* (witch hazel)-derived ingredients. The general lack of irritation and sensitization of these ingredients was noted. Because these ingredients are astringents and therefore may be irritating, and because they may be used in products applied near the eyes and mucous membranes, the Panel specified that products containing *Hamamelis virginiana* (witch hazel)-derived ingredients must be formulated to be non-irritating.

The Panel noted the lack of DART and repeated dose studies. Because of the reported composition of these ingredients, the Panel was not concerned about systemic toxicity or reproductive and developmental effects at the concentrations used in cosmetics. Additionally, *Hamamelis virginiana* (witch hazel)-derived substances have been used in OTC products at concentrations much higher than those reported for cosmetics, and they have a long history of human use without significant systemic toxicity. In addition, there was no concern about carcinogenicity because the results of in vitro genotoxicity studies and dermal and subcutaneous carcinogenicity studies were negative.

The Panel noted that, because botanical ingredients themselves are complex mixtures, there is concern that multiple botanical ingredients in one formulation may each contribute to the final concentration of a single shared constituent. Therefore, when formulating products, manufacturers should avoid reaching levels, in final formulations, of botanical constituents that may cause sensitization or other adverse effects. For example, geraniol and the oxidation products of linalool may be present in *Hamamelis virginiana* (witch hazel)-derived ingredients, as well as in other botanical ingredients. While these constituents are present in *Hamamelis virginiana* (witch hazel)-derived ingredients at concentrations below levels of concern, formulations with other botanical ingredients that share these constituents may lead to an effectively higher concentration in the final formulation which could result in potential dermal sensitization. The Panel noted that IFRA standards to avoid adverse effects have been published for several such constituents found in *Hamamelis virginiana* (Table 5).

Also, these ingredients are reported to be supplied as pre-formulations that may include solvents and preservatives. Cosmetics manufacturers and formulators are advised to be aware of the presence of potentially sensitizing components in

these mixtures, as supplied, and to avoid reaching levels of potential sensitizers that may be hazardous to consumers, especially when combining these ingredients with other ingredients that may contain the same potential sensitizers. CIR reports on the additional components of such pre-formulations should be consulted to identify any use recommendations that should be followed when formulating final cosmetic products.

The Panel expressed concern about pesticide residues, heavy metals, and substances from plants of other species (weeds) that may be present in botanical ingredients. To address these concerns, the cosmetics industry should continue to use current good manufacturing practices (cGMP) to limit impurities.

The Panel discussed the issue of incidental inhalation exposure. Some of the *Hamamelis virginiana* (witch hazel)-derived ingredients are used in cosmetics that could possibly be inhaled; for example, Hamamelis Virginiana (Witch Hazel) Water is reportedly used at concentrations up to 25.8% in body and hand products that are sprayed and at up to 0.93% in loose powder products that may become airborne. There were no inhalation toxicity data available. However, the Panel noted that 95% to 99% of droplets/particles 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, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic toxicological effects. The Panel considered other data available to characterize the potential for *Hamamelis virginiana* (witch hazel)-derived ingredients to cause toxicity, and noted the lack of systemic toxicity, genotoxicity, irritation, and sensitization at relevant doses of *Hamamelis virginiana* (witch hazel)-derived ingredients. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at http://www.cir-safety.org/cir-findings.

CONCLUSION

The CIR Expert Panel concluded that the following ingredients are safe in cosmetics in the present practices of use and concentration described in this safety assessment when formulated to be non-irritating and non-sensitizing:

Hamamelis Virginiana (Witch Hazel) Bark/Leaf Extract*
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract
Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract*
Hamamelis Virginiana (Witch Hazel) Extract
Hamamelis Virginiana (Witch Hazel) Flower Water
Hamamelis Virginiana (Witch Hazel) Leaf Extract
Hamamelis Virginiana (Witch Hazel) Leaf Water
Hamamelis Virginiana (Witch Hazel) Water

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

TABLES

Table 1. Definitions and functions of the *Hamamelis virginiana* (Witch Hazel)-derived ingredients.[1]

Ingredient	Definition	Functions
Hamamelis Virginiana (Witch Hazel) Bark/Leaf Extract [84696-19-5 (generic)]	Hamamelis Virginiana (Witch Hazel) Bark/Leaf Extract is the extract of the bark and leaves of *Hamamelis virginiana.*	Cosmetic astringent; skin-conditioning agent – miscellaneous
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract 84696-19-5 [(generic)]	Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract is the extract of the bark, leaves and twigs of *Hamamelis virginiana.*	Cosmetic astringent; skin-conditioning agent – miscellaneous
Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract [84696-19-5 (generic)]	Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract is the extract of the bark and twigs of *Hamamelis virginiana.*	Cosmetic astringent; skin-conditioning agent – miscellaneous
Hamamelis Virginiana (Witch Hazel) Extract 84696-19-5 [(generic)]	Hamamelis Virginiana (Witch Hazel) Extract is the extract of the whole plant, *Hamamelis virginiana*	Cosmetic astringent; skin-conditioning agent – miscellaneous
Hamamelis Virginiana (Witch Hazel) Flower Water [84696-19-5 (generic)]	Hamamelis Virginiana (Witch Hazel) Flower Water is an aqueous solution of the steam distillate obtained from the flowers of *Hamamelis virginiana.*	Fragrance ingredient
Hamamelis Virginiana (Witch Hazel) Leaf Extract [84696-19-5 (generic)]	Hamamelis Virginiana (Witch Hazel) Leaf Extract is the extract of the leaves of *Hamamelis virginiana.*	Cosmetic astringent; skin-conditioning agent – miscellaneous
Hamamelis Virginiana (Witch Hazel) Leaf Water [84696-19-5 (generic)]	Hamamelis Virginiana (Witch Hazel) Leaf Water is an aqueous solution of the steam distillates obtained from the leaves of *Hamamelis virginiana.*	Cosmetic astringent; skin-conditioning agent – miscellaneous
Hamamelis Virginiana (Witch Hazel) Water [84696-19-5 (generic)]	Hamamelis Virginiana (Witch Hazel) Water is an aqueous solution containing natural volatile oils obtained by the distillation of twigs, bark and leaves of *Hamamelis virginiana.*	Drug astringent – skin protectant drugs; skin-conditioning agent - miscellaneous

Table 2. Physical and chemical properties of trade name mixtures of *Hamamelis virginiana* (witch hazel)-derived ingredients.

Property	Value	Reference
Trade name mixture: 85% - 86% Hamamelis Virginiana (Witch Hazel) Leaf Water and 14% - 15% alcohol		
Physical Form	Liquid	13,28
Color	Clear	28
	Colorless to slight yellow	13
Odor	Characteristic	28
	Characteristic with slight green note	13
Specific Gravity @ 20°C	0.976 - 0.982	13,28
@ 25°C	0.979 - 0.983	13,28
Vapor pressure mmHg @ 20°C	18.75	28
Vapor Density mmHg	1.03	28
Melting Point °C	-8	28
Boiling Point °C	88	28
Water Solubility	Very soluble	28
Trade name mixture: 85% - 86% Hamamelis Virginiana (Witch Hazel) Water and 14% - 15% alcohol		
Physical Form	Liquid	14,30-34
Color	Clear	14,30-34
Odor	Characteristic	14,30-34
	Mild	34
Specific Gravity @ 20°C	0.976 - 0.982	30-34
@ 25°C	0.979 - 0.983	30-34
Vapor pressure mmHg @ 20°C	18.75	32,33
Vapor Density mmHg	1.03	32,33
Melting Point °C	-8	32,33
Boiling Point °C	88	32,33
Water Solubility g/L	Very soluble	32,33

Table 3. The constituents in the volatile fraction of water distilled (4 h) leaves and bark from freshly harvested *Hamamelis virginiana* (witch hazel) using *n*-hexane as the collector solvent, identified by GC-MS.[2]

Compound	Leaf (%)	Bark (%)
Hydrocarbons		
Alkanes, alkenes		
Octane	0.59	1.47
Nonane	0.01	0.02
Decane	0.01	0.04
Undecane	-	0.02
4,8-Dimethyl-1,3,7-nonatriene	-	0.07
Dodecane	0.03	0.1
Tridecane	0.54	trace
Tetradecane	0.23	0.2
3-Methyltetradecane	0.27	-
Pentadecane	0.1	minor
4,8,12-Trimethyl-1,3,7-tridecatetraene	0.23	0.13
Hexadecane	0.07	0.39
Not identified	0.13	-
1-Hexadecyne	0.16	-
Heptadecadiene	-	0.78
1-Heptadecene	-	0.05
Heptadecane	0.31	0.5
1-Octadecene	-	0.14
Octadecane	0.12	0.71
1-Nonadecene	-	0.31
Nonadecane	0.78	1.64
Eicosane	0.6	1.14
1-Heneicosene	-	0.14
Heneicosane	trace	4.78
2-Methylheneicosane	0.02	-
3-Methylheneicosane	0.01	-
1-Docosene	-	0.05
Docosane	1.27	0.87
Methyldocosane	0.05	0.04
2-Methyldocosane	0.02	0.04
Tricosane	10.38	3.14
Methyltricosane	0.02	-
Not identified	0.35	-
5-Methyltricosane	-	0.04
1-Tetracosene	0.08	0.06
Tetracosane	2.59	1,64
Methyltetracosane	0.03	-
Methyltetracosane	0.07	0.05
Methyltetracosane	0.01	-
4-Methyltetracosane	0.02	-
Methyltetracosane	0.07	-
Pentacosane	10.99	3.56
4-Methylpentacosane	0.05	-
2-Methylpentacosane	0.18	-
3-Methylpentacosane	0.15	-
1-Hexacosene	-	0.07
Hexacosane	2.27	1.92
Methylhexacosane	0.05	-
2-Methylhexacosane	0.22	0.15
3-Methylhexacosane	0.04	-
Heptacosane	16.12	5.45
3-Methylheptacosane	0.08	0.07
Ethyltetracosanoate	0.09	-
Octacosane	1.75	1.65
Methyloctacosane	0.03	-
2-Methylhexacosane	0.22	0.15
3-Methylhexacosane	0.04	-
Heptacosane	16.12	5.45
3-Methylheptacosane	0.08	0.07
Ethyltetracosanoate	0.09	-
Octacosane	1.75	1.65
Methyloctacosane	0.03	-
2-Methyloctacosane	0.07	-
3-Methyloctacosane	0.08	-
Nonacosane	7.12	6.86

Table 3. The constituents in the volatile fraction of water distilled (4 h) leaves and bark from freshly harvested *Hamamelis virginiana* (witch hazel) using *n*-hexane as the collector solvent, identified by GC-MS.[2]

Compound	Leaf (%)	Bark (%)
Methylnonacosane	0.09	0.18
Triacontane	1.14	1.96
2-Methyltriacontane	0.13	-
3-Methyltriacontane	0.04	-
Hentriacontane	1.14	2.24
Methylhentriacontane	0.06	-
Dotriacontane	0.69	0.98
Triatriacontane	0.68	1.01
Tetratriacontane	0.3	0.76
Sum	62.85	45.42
Alcohols		
cis-3-Hexenol	0.19	0.1
1-Hexanol	0.13	1.33
1-Heptanol	-	0.32
1-Octen-3-ol	0.03	1.16
3-Octanol	-	0.11
1-Octanol	Minor	-
1-Nonanol	0.09	0.6
1-Pentadecanol	-	0.05
1-Hexadecanol	0.1	0.05
1-Octadecanol	Minor	0.34
Eicosanol	0.02	1.25
Not identified	0.09	-
1-Docosanol	0.21	-
Sum	0.86	5.31
Aldehydes		
Octanal	0.03	-
Nonanal	0.62	2.72
2,6-Nonadienal	-	0.05
2-Nonenal (*cis* or *trans*)	-	0.01
Decanal	0.03	0.67
Undecanal	0.42	0.36
trans-2-Undecenal	0.03	0.36
Dodecanal	0.2	0.14
Tridecanal	0.24	0.41
Tetradecanal	0.05	0.07
Pentadecanal	0.13	0.12
Hexadecanal	0.15	0.15
Nonadecanal	0.03	0.09
Eicosanal	Trace	0.1
Heneicosanal	-	0.02
Docosanal	0.28	0.3
Tetracosanal	0.39	0.28
Hexacosanal	0.91	0.17
Octacosanal	0.28	0.12
Sum	3.79	6.14
Ketones		
2-Undecanone	-	0.02
γ-Nonalactone	-	0.03
2-Tridecanone	0.04	0.01
6-Methyl-5-(3-methylphenyl)-2-hepanone	-	Minor
5,9-Dimethyl-2-decanone	-	0.03
2-Pentadecanone	0.04	0.02
2-Hexadecanone	-	0.03
6,10,14-Trimethylpentadecan-2-one	0.7	0.68
2-Heptadecanone	0.05	0.08
γ-Hexadecalactone	-	0.04
2-Octadecanone	-	0.05
2-Nonadecanone	-	0.19
2-Eicosanone	-	0.02
2-Heneicosanone	-	0.29
2-Tricosanone	-	0.06
Sum	0.83	1.55

Table 3. The constituents in the volatile fraction of water distilled (4 h) leaves and bark from freshly harvested *Hamamelis virginiana* (witch hazel) using *n*-hexane as the collector solvent, identified by GC-MS.[2]

Compound	Leaf (%)	Bark (%)
Esters		
Methyl salicylate	-	0.02
cis-3-Hexenyl butyrate	Trace	-
trans-2-Hexenyl butyrate	0.14	-
cis-3-Hexenyl 2- or 3-methylbutyrate	0.15	0.24
cis-3-Hexenyl tiglate or angelate	0.06	0.02
Hexyl tiglate	Trace	0.02
Butyl benzoate	Trace	-
cis-3-Hexenyl hexanoate	0.23	-
trans-2-Hexenyl hexanoate	0.03	-
cis-3-Hexenyl *trans*-2-hexenoate	Trace	-
2-Methyl- or 3-methyl butylbenzoate	-	0.02
trans-2-Hexenyl *trans*-2-hexenoate	0.02	-
cis-3-Hexenyl benzoate	0.3	Trace
Hexyl benzoate	-	Trace
cis-3-Hexenyl octanoate	Trace	-
cis-3-Hexenyl salicylate	0.01	-
Benzyl benzoate	0.01	0.06
2-Phenylethyl benzoate	-	0.21
Sum	0.95	0.59
Terpenoids		
Monoterpenes		
cis-Linalool oxide (furanoid)	0.31	1.89
trans-Linalool oxide (furanoid)	0.12	0.5
Linalool	3.71	2.03
Hotrienol	Trace	Trace
Myrcenol	0.04	-
trans-Pinocarveol	-	0.06
Not identified	0.03	-
Nerol oxide	0.09	-
Not identified	0.12	-
Isoborneol	-	0.38
4-Terpineol	-	Minor
p-Cymen-8-ol	Trace	Trace
α-Terpineol	1.06	0.44
Myrtenol	-	0.3
Nerol	0.03	0.39
Isobornyl formate	-	Trace
Geraniol	1.74	1.21
Not identified	-	0.53
Geranyl formate	0.01	-
Geranylacetone	0.07	0.61
Sum	7.36	8.34

Table 3. The constituents in the volatile fraction of water distilled (4 h) leaves and bark from freshly harvested *Hamamelis virginiana* (witch hazel) using *n*-hexane as the collector solvent, identified by GC-MS.[2]

Compound	Leaf (%)	Bark (%)
Sesquiterpene hydrocarbons		
Cyclosativene	0.07	Trace
α-Ylangene	-	11.1
Sesquiterpene hydrocarbon	-	0.8
Sesquiterpene hydrocarbon	0.07	-
β-Caryophyllene	0.21	-
Sesquiterpene hydrocarbon	-	Trace
cis-α-Bergamotene	-	0.18
α-Humulene	0.05	-
α-Himachalene	-	0.04
Sesquiterpene hydrocarbon	-	0.03
β-Santalene	0.03	-
(*E*)-β-Farnesene	-	0.06
α-Amorphene	-	2.02
α-Curcument	-	Minor
α-Fanesene	0.08	-
Germacrene-D	-	0.16
(*E*,*E*)-α-Farnesene	1.47	-
β-Bisabolene	-	Minor
(*Z*)-γ-Bisabolene	-	1.08
δ-Calacorene	-	0.25
β-Calacorene	-	Minor
Cadalene	0.05	0.35
Sum	2.07	15.35
Oxygenated sesquiterpenes		
Not identified	-	0.15
trans-Nerolidol	0.17	2.73
Oxygenated sesquiterpene	-	0.08
Viridiflorol or ledol	0.21	-
α-Eudesmol	0.05	1.32
γ-Eudesmol	0.02	-
Gossonorol	-	0.23
α-Turnerone	0.8	-
τ-Muurolol	-	0.16
Not identified	-	0.16
Not identified	-	Trace
Sum	1.25	4.83
Diterpenes		
Manoyl oxide	0.03	0.93
Geranyl linalool-isomer-4[a]	0.47	-
Kaurene	0.02	-
Manool	0.1	-
Sum	0.62	0.99
Compounds with 13 carbons		
Vitispirane (*cis* and *trans*)	0.09	0.29
Rieslingacetal	Trace	Trace
1,1,6-Trimethyl-1,2-dihydronaphthalene	0.21	-
1,1,6-Trimethyl-1,2,3,4-tetrahydronaphthalene	0.01	-
trans-β-Damascenone	Trace	-
Hydroxydihydroedulan-1[a]	Trace	0.19
Sum	0.31	0.48
Phenylpropanoids		
Estragol	-	1.63
trans-Anethole	-	3.3
Eugenol	-	2.41
Methyleugenol	-	0.12
trans-Methylisoeugenol	-	Minor
Sum	-	7.46

Table 3. The constituents in the volatile fraction of water distilled (4 h) leaves and bark from freshly harvested *Hamamelis virginiana* (witch hazel) using *n*-hexane as the collector solvent, identified by GC-MS.[2]

Compound	Leaf (%)	Bark (%)
Fatty acids and fatty acid esters		
Nonanoic acid	0.11	0.09
Methyl tetradecanoate	0.03	0.01
Ethyl tetradecanoate	0.01	-
Isopropyl tetradecanoate	0.07	-
Methyl hexadecanoate	0.33	0.05
Hexadecanoic acid	1.62	0.03
Ethyl hexadecanoate	0.16	0.02
Methyl linolate	0.09	-
Methyl linolenate	0.47	Trace
Methyl oleate	0.13	-
Ethyl linolate	0.14	-
Ethyl linolenate	0.05	-
Methyl eicosanoate	0.04	-
Methyl docosanoate	0.11	-
Methyl tetracosanoate	0.15	-
Sum	3.57	0.20
Miscellaneous compounds		
2-Phenylacetaldehyde	-	0.02
1,4-Dimethyoxybenzene	-	Trace
Not identified	0.36	-
Not identified	0.02	0.45
Not identified	0.18	0.04
Dimethylnaphthalene[b]	-	0.06
Not identified	Trace	-
Butylhydroxytolene[b]	-	0.04
β-ionone	0.08	0.07
Not identified	0.25	-
Not identified	0.26	-
Tributylphosphate[b]	-	0.15
Phenanthrene[b]	0.01	0.19
Diisobutyl phthalate	0.01	0.01
Methylanthracene or Methylphenanthrene[b]	-	0.01
Dibutyl phthalate[b]	0.07	0.33
Fluoranthene or Pyrene[b]	-	0.05
Isophytol	0.68	0.05
trans-Phytol	9.79	-
Not identified	0.34	0.03
Not identified	0.18	-
Not identified	0.06	-
Not identified	0.14	0.28
Dioctyl phthalate[b]	-	Trace
Not identified	0.23	-
Not identified	0.16	0.05
Not identified	0.71	-
Not identified	0.33	-
Squalene	0.09	0.31
Sum	14.03	2.14
Total	98.48	98.8

[a] No further information was provided on the chemical
[b] Compound is probably a contaminant.
GC-MS = Gas chromatography-mass spectrometry; Minor = minor component of a peak comprised of more than one compound as estimated by MS; Trace = < 0.01%

Table 4. Constituents of concern found in *Hamamelis virginiana* (witch hazel)

Constituent	Concern	Reference
Geraniol	Potential dermal sensitizer	[4]
Linalool	Hydroperoxides are potential dermal sensitizers. Safe at up to 4.3% (20% in a consumer fragrance)	[3]
Phenol	Toxic by ingestion, inhalation, and dermal absorption. Strong dermal irritant. May induce cardiac arrhythmia and is toxic to the liver and kidneys.	[70,71]
Quercetin	Positive genotoxic effect in an Ames assay Consistently genotoxic in in vitro tests and in some in vivo studies of i.p. exposures, but was consistently nongenotoxic in oral exposure studies	[72,73]
Safrole	Liver cancer (hepatocellular carcinoma, adenoma) in male mice; liver cancer and other tumors in rats.	[74]

Table 5. Constituents of *Hamamelis virginiana* (witch hazel) that have IFRA standards.[18]

Constituent	Standard Limits
2-Phenylacetaldehyde	Limited to 0.01% - 2.9%, depending on use category due to sensitization.*
Benzyl benzoate	Limited to 2% - 42.8%, depending on use category due to sensitization.*
trans-β-Damascenone	Limited to 0.2% in fragrances and Eau de Toilette; 0.01% in other leave-on and rinse-off products; and 0.2% in non-skin, and incidental skin contact products due to carcinogenicity.
Estragol	Limited to 0.2% - 4.3%, depending on use category due to sensitization.*
Eugenol	Limited to 0.2% - 4.3%, depending on use category due to sensitization.*
Geraniol	Limited to 0.03% - 8.6%, depending on use category due to sensitization.*
Ionone (mixed isomers)	Limited to 2% - 50.72%, depending on use category due to sensitization.*
Linalool	Limit peroxide level to 20 mmol/L due to sensitization. Linalool and natural products known to be rich in linalool, such as bois de rose, coriander or ho wood oil, should only be used when the level of peroxides is kept to the lowest practical level. It is recommended to add antioxidants at the time of production of the raw material. The addition of 0.1% BHT or alpha-tocopherol for example has shown great efficiency. The maximum peroxide level for products in use should be 20 mmol/L.
Phenylacetaldehyde	Limited to 0.02% - 3%, depending on use category due to sensitization.*
Safrole	Not to be used as a fragrance ingredient. Essential oils containing safrole should not be used at a level such that the total concentration of safrole exceeds 0.01% in consumer products.

IFRA - International Fragrance Association

* Use categories are based on types of skin contact (e.g., skin, lips), length of contact (e.g., leave-on, rinse-off), or type of use (e.g., mouthwash)

Table 6. The contents of two product mixtures that contain Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract.[19-22]

	A	B
Mixture constituent	%	%
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract	10.00	20.00
Water	89.40	31.50
Propylene glycol	0	48.00
Phenoxyethanol	0.362	0.362
Tetrasodium EDTA	0.10	0
Methylparaben	0.078	0.078
Ethylparaben	0.02	0.02
Butylparaben	0.02	0.02
Propylparaben	0.01	0.01
Isobutylparaben	0.01	0.01

Table 7. Allergens certified to not be present in product mixtures containing 10% or 20% Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig or 5.00% Hamamelis Virginiana (Witch Hazel) Extract. [19,21,25]

Allergen	Limit of Detection (ppm)
α-Isomethyl ionone	< 0.02
Amyl cinnamal	< 0.10
Amylcinnamyl alcohol	< 1.00
Anise alcohol	< 0.00
Benzyl alcohol	< 0.01
Benzyl benzoate	< 0.09
Benzyl cinnamate	< 0.30
Benzyl salicylate	< 0.06
Butylphenyl methylpropional	< 0.50
Cinnamal	< 0.01
Cinnamyl alcohol	< 0.30
Citral	< 1.00
Citronellol	< 1.00
Coumarin	< 0.00
Eugenol	< 0.70
Farnesol	< 0.04
Geraniol	< 0.08
Hexyl cinnamal	< 0.40
Hydroxycitronellal	< 1.00
Hydroxymethylpentyl 3-cyclohexene carboxaldehyde	< 0.30
Isoeugenol	< 0.06
Limonene	< 0.05
Linalool	< 0.00
Methyl 2 octynoate	< 0.02
Evernia furfuracea	< 0.00

Table 8. Frequency of use according to duration and exposure of *Hamamelis virginiana* (witch hazel)-derived ingredients.[36,37]

Use type	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)
	Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract		Hamamelis Virginiana (Witch Hazel) Extract		Hamamelis Virginiana (Witch Hazel) Flower Water		Hamamelis Virginiana (Witch Hazel) Leaf Extract[f]	
Total/range	**125**	**0.00005-4.3**	**393**	**0.000013-1.8**	**39**	**NR**	**218**	**0.00018-0.011**
Duration of use								
Leave-on	89	0.00005-4.3	305	0.00003-1.8	18	NR	143	0.00018-0.011
Rinse-off	35	0.00005-0.072	86	0.000013-1.8	20	NR	68	0.00035-0.01
Diluted for (bath) use	1	NR	2	0.000013-0.0001	1	NR	7	NR
Exposure type								
Eye area	14	NR	18	0.1	3	NR	11	NR
Incidental ingestion	1	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-sprays	23[a]; 26[b]	0.18[a]	2; 95[a]; 138[b]	0.00003-0.03; 0.0013[a]	4[a]; 6[b]	NR	1; 43[a]; 64[b]	0.00035[a]
Incidental inhalation-powders	NR	0.004-4.3[c]	1; 138[b]	0.0001-1.8[c]	NR	NR	1; 64[b]	0.0018-0.011[c]
Dermal contact	121	0.00005-4.3	383	0.000013-1.8	39	NR	199	0.00018-0.011
Deodorant (underarm)	3[a]	NR	4[a]	0.0013[d]; 0.0013[e]	NR	NR	6[a]	0.00018[d]
Hair-noncoloring	1	NR	7	0.0001-0.3	NR	NR	19	0.00035-0.00042
Hair-coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	2	NR	2	NR	NR	NR	NR	NR
Mucous Membrane	6	NR	12	0.000013-1	7	NR	21	NR
Baby	1	NR	NR	NR	NR	NR	NR	NR

	Hamamelis Virginiana (Witch Hazel) Leaf Water		Hamamelis Virginiana (Witch Hazel) Water		Hamamelis Virginiana (Witch Hazel) Bark Extract[g]		Witch Hazel[g]	
Total/range	**NR**	**0.67-4.1**	**376**	**0.00008-43**	**1**	**NS**	**38**	**NS**
Duration of use								
Leave-on	NR	NR	244	0.00008-43	NR	NS	26	NS
Rinse-off	NR	0.67-4.1	122	0.00066-33.3	1	NS	10	NS
Diluted for (bath) use	NR	NR	10	0.43	NR	NS	2	NS
Exposure type								
Eye area	NR	NR	18	0.04-30.6	NR	NS	2	NS
Incidental ingestion	NR	NR	5	0.1-30.6	NR	NS	NR	NS
Incidental Inhalation-sprays	NR	NR	94[a]; 74[b]	0.00008-25.8; 0.00086-6.1[a]; 0.0086[b]	NR	NS	2; 8[a]; 5[b]	NS
Incidental inhalation-powders	NR	NR	2[c]; 74[b]	0.043-0.093; 0.00066-8.5[c]; 0.0086[b]	NR	NS	5[b]	NS
Dermal contact	NR	4.1-5	352	0.00008-43	1	NS	31	NS
Deodorant (underarm)	NR	NR	15[a]	0.086-5.2[d]	NR	NS	6[a]	NS
Hair-noncoloring	NR	NR	16	0.26-2.5	NR	NS	6	NS
Hair-coloring	NR	NR	NR	NR	NR	NS	NR	NS
Nail	NR	NR	1	4.3	NR	NS	1	NS
Mucous Membrane	NR	NR	45	0.0086-30.6	NR	NS	4	NS
Baby	NR	NR	4	NR	NR	NS	NR	NS

NR = Not Reported; NS = Not Surveyed; Totals = Rinse-off + Leave-on + Diluted for Bath Product Uses.
Note: Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure type uses may not equal the sum total uses.
[a] It is possible these products may be sprays, but it is not specified whether the reported uses are sprays.
[b] Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.
[c] It is possible these products may be powders, but it is not specified whether the reported uses are powders.
[d] Not spray.
[e] Spray.
[f] The VCRP had entries for "Witch Hazel Leaf Extract" and Hamamelis Virginiana (Witch Hazel) Leaf Extract, which are combined here.
[g] Listed in the VCRP but are not cosmetic ingredient names according to the wINCI *Dictionary*.

Table 9. In vitro genotoxicity assays of *Hamamelis virginiana* (witch hazel)-derived ingredients.

Ingredient/Test Substance	Concentration	Assay	Results	Reference
Product containing Hamamelis Virginiana Leaf Extract (6%)	Product: 333 – 66,666 µg/plate (0.06 – 3100 µg/plate Hamamelis Virginiana Leaf Extract) in water	Ames assay using *S. typhimurium* (TA98, TA00 [sic], TA1535, TA1537) and E. coli (WP2 uvrA)	Weak toxic effects were occasionally observed at approximately 33,333 µg/plate. No increase in the number of revertant colonies at any concentration for any strain with or without metabolic activation.	[46]
Hamamelis Virginiana (Witch Hazel) Water	Concentration not specified	*Salmonella* mammalian microsome assay (stains TA97, TA98, TA100, and TA1535)	Not genotoxic with and without metabolic activation	[5]
Hamamelis Virginiana (Witch Hazel) Water	Up to 5000 µg/mL	SCE	Negative with and without metabolic activation	[47]
Hamamelis Virginiana (Witch Hazel) Water	Up to 5000 µg/mL	Chromosome aberration test	Negative with and without metabolic activation	[47]
Hamamelis Virginiana (Witch Hazel) Water	Up to 5000 µg/mL	L5178Y tk+/- mouse lymphoma cell forward mutation assay. Cultures were exposed to test substance for 4 h, and cultured for 2 days before plating in soft agar with or without TFT(3 µg/mL). Negative control was distilled water; positive controls were methyl methanesulphonate without metabolic activation and ethyl methanesulphonate with metabolic activation. Test substance was tested at least twice.	Not a mutagen	[5,48]
Hamamelis virginiana (witch hazel) leaf oil (under the CAS number 68916-39-2)	100 to 10,000 µg/plate	Ames assay using *S. typhimurium* (stains TA98, TA100, TA1535, and TA1537)	Negative with and without metabolic activation	[49]

SCE = sister chromatid exchange; TFT = trifluorothymidine

Table 10. HRIPTs of *Hamamelis virginiana* (Witch Hazel)-derived ingredients.

Ingredient	Concentration	n	Procedure	Results	Reference
Hamamelis Virginiana (Witch Hazel) Leaf Extract	0.45% (trade name mixture containing 6% Hamamelis Virginiana (Witch Hazel) Leaf Extract diluted in water to 7.5%)	108	Test material was applied to upper back under semi-occlusion for 24 h for a total of 9 applications. After a two-week rest period, challenge patch was applied to a naive site for 24 h and test site was examined for signs of irritation or sensitization.	Negative for irritation and sensitization	[46]
Hamamelis Virginiana (Witch Hazel) Water	25.80%	105	Induction patches were applied neat to upper back three times per week for three weeks. Test sites were wiped with 70% isopropyl alcohol prior to placement of patches. Patches were in place for 24 h. Test sites were examined prior to application of next patch. After approximately 2 weeks rest, challenge patch was applied for 24 h. Challenge site was examined upon removal, and at 48 and 72 h. If there was a reaction, it was examined again at 96 h.	There were no reactions at any time during this test demonstrating no potential for irritation or sensitization of this test material.	[59]
Hamamelis Virginiana (Witch Hazel) Water	6.88%	199	Test material was applied neat to upper back under semi-occlusion for 24 h for a total of 9 applications. After a 10- to 15-day rest period, challenge patch was applied to a naive site for 24 h and test site was examined.	Negative for sensitization.	[60]
Hamamelis Virginiana (Witch Hazel) Water	6.02%	107	Patches were applied neat to upper back after wiping test site with isopropyl alcohol for 24 h for a total of 9 applications. After an approximately 2-week rest period, challenge patch was applied to a naive site for 24 h and test site was examined for signs of irritation or sensitization at 24 and 72 h.	Negative for irritation and sensitization.	[61]

Table 11. *Hamamelis virginiana* (witch hazel)-derived ingredients administered to damaged skin.

Ingredient	Dose, vehicle	Procedure/notes	Results	Reference
Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract	Creams with and without Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract (10%)	Skin on subjects' backs (n = 28; skin types I, II, or III) was exposed to UV light (mainly in the UVB range with a small amount of UVA and visible light) at 1, 1.25, 1.6, and 2 MED. Test substances were administered using 18-mm Finn chambers immediately after and at 7 and 24 h after irradiation. Test sites were observed at 7, 24 and 48 h after irradiation.	There were no adverse events reported at any time during the experiment.	[65]
Hamamelis virginiana (witch hazel) distillate (plant parts not specified)	0.00064% (0.64 mg *Hamamelis* ketone/100 g; 75 µL applied) o/w emulsion with and without PC; 0.00256% (2.56 mg *Hamamelis* ketone/100 g; 75 µL applied). Controls were the vehicles and an untreated area.	Randomized, double-blind studies. EXPERIMENT 1: Skin on subjects' backs (n=24) was exposed to UV light (mainly in the UVB range with a small amount of UVA and visible light) at 1.5 MED then test substances were applied. Test sites were observed at 24 and 48 h. EXPERIMENT 2: Skin subjects' backs (n=12) was tape stripped. The low-dose (0.00064% without PC) emulsion and the vehicle (control) were applied. Skin on another group of subjects backs (n=12) was tape stripped. The low- and high-dose (0.00064% and 0.00256% with PC) emulsions were applied. Vehicles were the controls. Test sites were observed at 4, 8 and 24 h.	There were no adverse effects observed in any group during the experiments.	[66]
Hamamelis virginiana (witch hazel) distillates (plant parts and composition not specified) from three different suppliers	O/W emulsions containing a *Hamamelis virginiana* (witch hazel) distillate (10%) from three different suppliers	Double-blind study. Skin on light-skinned subjects backs (n = 40) was exposed to a sun simulator (UVA:UVB, 16:1; 4 mW/cm^2 UVB) at 1.2, 1.4, and 1.7 MED. Test substances (250 µL) were administered using 18-cm Finn chambers immediately after and at 24 and 48 h after irradiation. Test sites were observed at 24, 48, and 72 h after irradiation.	There were no adverse events reported at any time during the experiment.	[67]
Hamamelis virginiana (witch hazel) distillate (plant parts not specified)	Creams containing *Hamamelis virginiana* (witch hazel) distillate (0.00064%; 0.64 mg *Hamamelis* ketone/100 g) with and without 0.5% hydrocortisone or just the vehicle	Randomized, double-blind study. Subjects (n = 72) with moderately severe atopic eczema applied a cream containing *Hamamelis virginiana* (witch hazel) distillate on one side of the body and either the same cream with hydrocortisone or the vehicle to lesions on the other side of the body twice per day for 14 days. Blood samples were collected before and after the experiment period at the discretion of a physician.	Self and physician scores of tolerability were similar to controls. Five subjects had itching, erythema, stinging, lichenification/dry skin from using the vehicle. One subject had signs of skin irritation from both the cream containing *Hamamelis virginiana* (witch hazel) distillate and the vehicle control. There were no adverse effects connected to the application of *Hamamelis virginiana* distillate.	[68]

MED = minimal erythema doses; o/w= oil/water; PC = phosphatidylcholine

REFERENCES

1. Nikitakis, J and Lange B (eds). Web-based International Cosmetic Ingredient Dictionary and Hanbook (wINCI). http://webdictionary.personalcarecouncil.org/jsp/Home.jsp. Washington, DC. Last Updated 2017. Date Accessed 5-2-2017.

2. Engel R, Gutmann M, Hartisch C, Kolodziej H, and Nahrstedt A. Study on the composition of the volatile fraction of *Hamamelis virginiana*. *Planta Medica*. 1998;64(3):251-258.

3. Bickers D, Calow P, Greim H, Hanifin JM, Rogers AE, Saurat JH, Sipes IG Smith RL, and Tagami H. A toxicologic and dermatologic assessment of linalool and realated esters when used as fragrance ingredients. *Food and Chemical Toxicology*. 2003;41(7):919-942.

4. Nijkamp MM, Bokkers BG, Bakker MI, Exendam J, and Delmaar JE. Quantitiative risk assessment of the aggregate dermal exposure to the sensitizing fragrance geraniol in personal care products and household cleaning products. *Regulatory Toxicology and Pharmacology*. 2015;73(1):9-18.

5. Committee on Herbal Medicinal Products (HMPC). Assessment report on *Hamamelis virginiana* L., cortex *Hamamelis virginiana* L., folium *Hamamelis virginiana* L., folium et cortex aut ramunculus destillatum. Canary Wharf, London, European Medicines Agency (EMA). 2009. http://www.ema.europa.eu/docs/en_GB/document_library/Herbal_-_HMPC_assessment_report/2010/04/WC500089242.pdf. Report No. EMA/HMPC/114585/2008. pp. 1-47.

6. European Agency for the Evaluation of Medicinal Products (EMEA), Veterinary Medicines Evaluation Unit. Hamamelis virginiana summary report (1). Canary Wharf, London, European Medicines Agency. 1998. http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500014389.pdf. Report No. EMEA/MRL/358/98-FINAL. pp. 1-2.

7. World Health Organization (WHO). Folium et Cortex Hamamelidis. In: *WHO Monographs on Selected Medicinal Plants - Volume 2*. Vol. 2. Geneva: 2002:124-136.

8. Weber, RW. Allergen of the month - Witch hazel. *Annals of Allergy, Asthma, & Immunology*. 2012;109(5):A17

9. Anderson GJ and Hill JD. Many to flower, few to fruit: The reproductive biology of *Hamamelis virginiana* (Hamamelidaceae). *Amercian Jounal of Botony*. 2002;89(1):67-78.

10. eFloras. Flora in North America: Hamamelis Linnaeus. *eFloras*. 2017. Missouri Botanical Garden, St.Louis, MO & Harvard University Herbiaraia, Cambridge, MA. http://www.efloras.org/florataxon.aspx?flora_id=1&taxon_id=114541Date Accessed 6-1-2017

11. Active Concepts. 2017. Manufacturing flow chart ABS Witch Hazel Extract (Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract). Unpublished data submitted by Personal Care Products Council.

12. Active Concepts. 2017. Manufacturing flow chart ABS Witch Hazel Extract Sil (Hamamelis Virginiana (Witch Hazel) Extract). Unpublished data submitted by Personal Care Products Council.

13. American Distilling Inc. Specifications: Certified organic witch hazel leaf extract [pamphlet]. East Hampton, CT: American Distilling Inc; 2012.

14. American Distilling Inc.. Specifications: Distilled witch hazel (14% natural grain alcohol) [pamphlet]. East Hampton, CT: American Distilling Inc.; 2012.

15. Elias, J and Masline, SR. The A to Z Guide to Healing Herbal Remedies. 1 *ed*. New York: Lynn Sonberg Book Associates, 1995.

16. PDR for herbal medicines. 4 *ed*. Montvale, NJ: Thomson Healthcare, Inc., 2017.

17. Duke JA. Handbook of phytochmical constituents of GRAS herbs and other economic plants. Boca Raton, FL: CRC Press, 1992.

18. International Fragrance Association (IFRA). IFRA Standards. 2017. http://www.ifraorg.org/en-us/standards-library. Date Accessed 1-30-2017.

19. Active Concepts. 2017. Compositional breakdown ABS Witch Hazel Extract (Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract). Unpublished data submitted by Personal Care Products Council.

20. Active Concepts. 2017. Certificate of origin ABS Witch Hazel Extract (Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract). Unpublished data submitted by Personal Care Products Council.

21. Active Concepts. 2017. Compositional breakdown ABS Witch Hazel Extract NS (Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract). Unpublished data submitted by Personal Care Products Council.

22. Active Concepts. 2017. Certificate of origin ABS Witch Hazel Extract NS (Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract). Unpublished data submitted by Personal Care Products Council.

23. Active Concepts. 2017. Product specification ABS Witch Hazel Extract (Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract). Unpublished data submitted by Personal Care Products Council.

24. Active Concepts. 2017. Product specification ABS Witch Hazel Extract NS (Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract). Unpublished data submitted by Personal Care Products Council.

25. Active Concepts. 2017. Compositional breakdown ABS Witch Hazel Extract Sil (Hamamelis Virginiana (Witch Hazel) Extract). Unpublished data submitted by Personal Care Products Council.

26. Active Concepts. 2017. Certificate of origin ABS Witch Hazel Extract Sil (Hamamelis Virginiana (Witch Hazel) Extract). Unpublished data submitted by Personal Care Products Council.

27. Active Concepts. 2017. Product specification ABS Witch Hazel Extract Sil (Hamamelis Virginiana (Witch Hazel) Extract). Unpublished data submitted by Personal Care Products Council.

28. American Distilling Inc.. Material safety data sheet: Certified organic witch hazel leaf extract [pamphlet]. East Hampton, CT: American Distilling Inc; 2011.

29. United States Pharmacopeia and National Formulary (USP-NF). Witch hazel. http://www.uspnf.com/notices/witch-hazel. Last Updated 6-30-2017. Date Accessed 11-30-2017.

30. American Distilling Inc. Specifications: Distilled witch hazel (14% standard alcohol) [pamphlet]. East Hampton, CT: American Distilling Inc.; 2011.

31. American Distilling Inc.. Material safety data sheet: Distilled witch hazel (14% standard alcohol) [pamphlet]. East Hampton, CT: American Distilling Inc; 2011.

32. American Distilling Inc.. Material safety data sheet: Distilled witch hazel, AVF [pamphlet]. East Hampton, CT: American Distilling Inc; 2011.

33. American Distilling Inc.. Material safety data sheet: Distilled witch hazel 14% natural grain alcohol [pamphlet]. East Hampton, CT: American Distilling Inc.; 2011.

34. American Distilling Inc. Specifications: Distilled witch hazel, AVF [pamphlet]. East Hampton, CT: American Distilling Inc.; 2011.

35. Ramos MFS, Santos EP, Bizarri CHB, Mattos HA, Padilha MRS, and Duarte HM. Preliminary studies towards utilization of various plant extracts as antisolar agents. *International Journal of Cosmetic Science*. 1996;18(3):87-101.

36. U.S. Food and Drug Administration Center for Food Safety & Applied Nutrition (CFSAN). Voluntary Cosmetic Registration Program - Frequency of Use of Cosmetic Ingredients. College Park, MD, 2018. Obtained under the Freedom of Information Act from CFSAN; requested as "Frequency of Use Data" January 3 2018; received February 5 2018).

37. Personal Care Products Council. 10-16-2017. Updated Concentration of Use by FDA Product Category: Witch Hazel-Derived Ingredients. Unpublished data submitted by Personal Care Products Council.

38. Johnsen MA. The Influence of Particle Size. *Spray Technology and Marketing*. 2004;14(11):24-27. http://www.spraytechnology.com/index.mv?screen=backissues.

39. Rothe H. Special aspects of cosmetic spray safety evaluation. 2011. Unpublished information presented to the 26 September CIR Expert Panel. Washington D.C.

40. Bremmer HJ, Prud'homme de Lodder LCH, and van Engelen JGM. Cosmetics Fact Sheet: To assess the risks for the consumer; Updated version for ConsExpo 4. 2006. http://www.rivm.nl/bibliotheek/rapporten/320104001.pdf. Date Accessed 8-24-2011. Report No. RIVM 320104001/2006. pp. 1-77.

41. Rothe H, Fautz R, Gerber E, Neumann L, Rettinger K, Schuh W, and Gronewold C. Special aspects of cosmetic spray safety evaluations: Principles on inhalation risk assessment. *Toxicol Lett*. 8-28-2011;205(2):97-104. PM:21669261.

42. CIR Science and Support Committee of the Personal Care Products Council (CIR SSC). 11-3-2015. Cosmetic Powder Exposure. Unpublished data submitted by the Personal Care Products Council.

43. Aylott RI, Byrne GA, Middleton, J, and Roberts ME. Normal use levels of respirable cosmetic talc: preliminary study. *Int J Cosmet Sci*. 1979;1(3):177-186. PM:19467066.

44. Russell RS, Merz RD, Sherman WT, and Sivertson JN. The determination of respirable particles in talcum powder. *Food Cosmet Toxicol*. 1979;17(2):117-122. PM:478394.

45. Qinna NA. Safety profile of suppository *Hemamelis virginiana* leaf extract. *Journal of Medicinal Plants Research*. 2013;7(36):2669-2679.

46. BASF. 2015. Information on toxicological data for a trade name mixture containing Hamamelis Virginiana Leaf Extract. Unpublished data submitted by Personal Care Products Council.

47. Galloway SM, Armstrong MJ, Reuben C, Colman S, Brown B, Cannon C, Bloom AD, Nakamura F, Ahmed M, Duk S, Rimpo J, Margolin BH, Resnick MA, Anderson B, and Zeiger E. Chromosome aberrations and sister chromatid exchages in Chinese hamster ovary cells: Evaluations of 108 chemicals. *Environmental and Molecular Mutagenesis*. 1987;10(Supplement 10):1-175.

48. McGregor DB, Brown A, Cattanach P, Edwards I, McBride D, and Caspary WJ. Responses of the L5178Y tk^+/tk^- mouse lymphoma cell forward mutation assay II; 18 coded chemicals. *Environmental and Molecular Mutagenesis*. 1988;11(1):91-118.

49. Mortelmans, K, Haworth, S, Lawlor, T, Speck, W, Tainer, B, and Zeiger E. Salmonella mutagenicty tests: II. Results from the testing of 270 chemicals. *Environmental Mutagenesis*. 1986;8(Suppl. 7):1-119.

50. Board of Scientific Counselors, National Toxicology Program (NTP). Summary minutes from peer reviews of draft technical reports of long-term toxicology and carcinogenesis studies by the Technical Reports Review Subcommittee and Pane of Experts. Washington, DC, National Toxicology Program (NTP). 3-23-1984. pp. 1-11.

51. Haseman JK, Crawford DD, Huff JE, Boorman GA, and McConnell EE. Results from 86 two-year carcinogenicity studies conducted by the National Toxicology Program. *Journal of Toxicology and Environmental Health*. 1984;14:621-639.

52. Haseman JK, Huff JE, Zeiger E, and McConnell EE. Comparative results of 327 chemical carcinogenicity studies. *Environmental Health Perspectives*. 1987;74:229-235.

53. Kapadia GJ, Chung EB, Ghosh B, Shukla YN, Basak SP, Morton JF, and Pradhan SN. Carcinogenicity of some folk medicinal herbs in rats. *Journal of the National Cancer Institute*. 1978;60(3):683-686.

54. Clinical Research Laboratories Inc. 2006. Safety-in-use study to determine the ocular and dermal irritation potential and comedogenic-acnegenic potential of a cosmetic product (sunless tanner containing 6.02% Hamamelis Virginiana (Witch Hazel) Water). Unpublished data submitted by Personal Care Products Council.

55. Active Concepts. 2017. Dermal and ocular irritation tests ABS Witch Hazel Extract NS (Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract). Unpublished data submitted by Personal Care Products Council.

56. Active Concepts. 2017. Dermal and ocular irritation tests ABS Witch Hazel Extract (Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract). Unpublished data submitted by Personal Care Products Council.

57. Active Concepts. 2017. Dermal and ocular irritation tests ABS Witch Hazel Extract Sil (Hamamelis Virginiana (Witch Hazel) Extract). Unpublished data submitted by Personal Care Products Council.

58. Anonymous. 2015. Summary of study of acute compatibility of a test item: 48-hours occlusive patch test of a face tonic with 8.5% Hamamelis Virginiana (Witch Hazel) Water. Unpublished data submitted by Personal Care Products Council.

59. Clinical Research Laboratories Inc. 2011. Repeated insult patch test of a soothing spray containing 25.80% Hamamelis Virginiana (Witch Hazel) Water. Unpublished data submitted by Personal Care Products Council.

60. TKL Research Inc. 2013. Repeated insult patch test of a toner containing 6.88% Hamamelis Virginiana (Witch Hazel) Water. Unpublished data submitted by Personal Care Products Council.

61. Clinical Research Laboratories Inc. 2006. Repeated insult patch test of a tanning spray containing 6.02% Hamamelis Virginiana (Witch Hazel) Water. Unpublished data submitted by Personal Care Products Council.

62. Wolff HH and Kieser M. Hamamelis in children with skin disorders and skin injuries: results of an observational study. *European Journal of Pediatrics*. 2007;166(9):943-948.

63. Paulsen E, Christensen LP, and Andersen KE. Cosmetics and herbal remedies with Compositae plant extracts - are they tolerated by Compositae-allergic patients? *Contact Dermatitis*. 2008;58(1):15-23.

64. Bruynzeel DP, van Ketel WG, Young E, van Joost T, and Smeenk G. Contact sensitization by alternative topical medicaments containing plant extracts. *Contact Dermatitis*. 1992;27(4):278-279.

65. Hughes-Formella BJ, Bohnsack K, Rippke F, Benner G, Rudolph M, Tausch I, and Gassmueller J. Anti-inflammatory effect of Hamamelis lotion in a UVB erythema test. *Dermatology*. 1998;196(3):316-322.

66. Korting HC, Schäfer-Korting M, Hart H, Laux P, and Schmid M. Anti-inflammatory activity of hamamelis distillate applied topically to the skin. *European Journal of Clinical Pharmacology*. 1993;44(4):315-318.

67. Hughes-Formella BJ, Filbry A, Gassmueller J, and Rippke F. Anti-inflammatory efficacy of topical preparations with 10% hamamelis distillate in a UV erythema test. *Skin Pharmacology and Applied Skin Physiology*. 2002;15(2):125-132.

68. Korting HC, Schäfer-Korting M, Klõvekorn W, Klõvekorn G, Martin C, and Laux P. Comparative efficacy of hamamelis distillate and hydrocortisone cream in atopic eczema. *European Journal of Clinical Pharmacology*. 1995;48(6):461-465.

69. Granlund H. Contact allergy to witch hazel. *Contact Dermatitis*. 1994;31(3):195

70. Hawley's Condensed Chemical Dictionary. 15 *ed*. Hoboken, NJ: John Wiley & Sons, Inc., 2007.

71. Lover CW. Chemexfoliation--indications and cautions. *Journal of the American Academy of Dermatology*. 1987;17(1):109-112.

72. Harwood M, Danielewska-Nikiel B, Borzelleca JF, Flamm GW, Williams GM, and Lines TC. A critical review of the data related to the safety of quercetin and lack of evidene of *in vivo* toxicity, including lack of genotoxic/carcinogenic properties. *Food and Chemical Toxicology*. 2007;45(11):2179-2205.

73. Poginsky B, Westendorf N, Prosenc N, Kuppe M, and Marquardt H. St. John's wort (*Hypericum perforatum* L.). Genotoxicity induced by quercetin content. *Deutsche Apotheker Zeitung*. 1988;128:13464-13466.

74. National Toxicology Program (NTP). 14th report on carcinogens (RoC) - Safrole CAS No. 94-59-7. Triangle Park, NC, National Institute of Environmental Health Sciences. 2016. http://ntp.niehs.nih.gov/ntp/roc/content/profiles/safrole.pdf. pp. 1-2.