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

Status:	Scientific Literature Review for Public Comment
Release Date:	July 7, 2017
Panel Meeting Date:	September 11-12, 2017

All interested persons are provided 60 days from the above date to comment on this safety assessment and to identify additional published data that should be included or provide unpublished data which can be made public and included. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient. All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a peer-reviewed scientific journal. Please submit data, comments, or requests to the CIR Interim Director, Dr. Bart Heldreth.

The 2017 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Interim Director is Bart Heldreth, Ph.D. This report was prepared by Lillian C. Becker, Scientific Analyst/Writer.

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INTRODUCTION

This is a review of the safety of 8 *Hamamelis virginiana* (witch hazel)-derived ingredients as used in cosmetics (Table 1). The ingredients in this group are derived from the *Hamamelis virginiana* (witch hazel) plant. According to the *Cosmetic Ingredient Dictionary and Handbook* (*Dictionary*), functions of most of the ingredients listed below include cosmetic astringent and skin-conditioning agent - miscellaneous.[1]

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

The *Dictionary* also lists drug astringent – skin protectant drug as a function of Hamamelis Virginiana (Witch Hazel) Water.[1] Drug astringent is not a cosmetic function, and the Cosmetic Ingredient Review (CIR) Expert Panel (Panel) does not evaluate non-cosmetic functions.

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 no. 68916-39-2); the taxonomic name is used unless it is clear that the test substance is similar to a cosmetic ingredient. If the tested substance is similar to a cosmetic ingredient, then the INCI name is used.

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.[2-4] Reports by these organizations are cited in this assessment to identify the source of the data obtained from these summaries.

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 and are potential dermal sensitizers.[5-7] 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.

The names of the ingredients in this report are written in accordance with the *Dictionary*, as shown above, 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*).

CHEMISTRY

Definition

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

Plant Identification

Hamamelis virginiana (witch hazel), 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.[2,4,8-10] 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. *Hamamelis virginiana* (witch hazel) likely reproduces through insect pollination instead of wind pollination. 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 capsule 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

Chemical and physical properties 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]

A manufacturer reports that one Hamamelis Virginiana (Witch Hazel) Leaf Water product is a distillate prepared from recently harvested and partially dried leaves of *Hamamelis virginiana* (witch hazel).[11] Alcohol is added to the final product at 14%. The same manufacturer reports that a different Hamamelis Virginiana (Witch Hazel) Water product is a distillate prepared from recently cut and partially dried dormant twigs of *Hamamelis virginiana* (witch hazel).[12] In this product, grain alcohol or ethanol is added to the final product at 14%.

Composition

Hamamelis virginiana (Witch Hazel) Plants

Constituents of the bark and leaves of *Hamamelis virginiana* (witch hazel) are presented in Table 3.

Polyphenols - The leaves contain up to, but not more than 3%, tannins.[4,13] 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.[4] Leaf tannins are a mixture of gallic acid (10%), hydrolysable 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 kaempherol, quercetin, quercitrin, and isoquercitrin.[2]

Catechins - Catechins include (+)-catechin, (+)-gallocatechin, (-)-epicatechin gallate(III), and (-)-epigallocatechin gallate(III). Oligomeric procyanidins are also present.[4,13]

Volatile oil – Both bark and leaves contain volatile oil (0.1% and 0.01%-0.05%, respectively).[3] The composition of the volatile fraction obtained by water distillation from the leaves and bark of *Hamamelis virginiana* (witch hazel), determined by gas chromatography-mass spectrometry (GC-MS), consists in about 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.[2] Other components include kaempferol, quercetin, chlorogenic acid isomers, and hydroxycinnamic acids.[4] 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* (witch hazel) using n-hexane as the collector solvent are listed in Table 4. The constituents were identified by GC-MS.[5]

Hamamelis virginiana (Witch Hazel)-Derived Ingredients

The method of manufacture significantly impacts the composition of the *Hamamelis virginiana* (witch hazel)-derived ingredients. For example, distilled ingredients have fewer astringent tannins than a water extract.[14]

Hamamelis Virginiana (Witch Hazel) Water is reported by a manufacturer to be supplied at 85%-86% with 14%-15% grain alcohol or ethanol.[15-17] The same manufacturer reports that Hamamelis Virginiana (Witch Hazel) Leaf Water is also supplied at 85%-86% with 14%-15% ethanol.[18]

Impurities/Constituents

Hamamelis virginiana (Witch Hazel)-Derived Ingredients

Specifications for Hamamelis Virginiana (Witch Hazel) Leaf Water (and 14% grain alcohol) states that this ingredient 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 negative for acetone, other ketones, isopropyl alcohol and *t*-butyl alcohol.[11]

Specifications for Hamamelis Virginiana (Witch Hazel) Water (and 14% grain alcohol) states that this ingredient is to contain < 25 mg/100 mL nonvolatile residue, < 10 CFU/mL yeast and mold, a maximum of 1 CFU/mL bacteria, and is negative for acetone, other ketones, isopropyl alcohol and t-butyl alcohol, and formaldehyde.[12,19,20] Tannins are limited to < 0.03 mg/mL.

Hamamelis virginiana (Witch Hazel)

Table 5 lists concerns of constituents of *Hamamelis virginiana* (witch hazel) plants. These plants are reported to contain linalool and quercetin.[5,21] Safrole was also found at a level of < 0.2% in *Hamamelis virginiana* (witch hazel) leaf oil.[2] Possible contaminants (e.g., tributylphosphate and dibutyl phthalate) from the volatile fraction of water-distilled leaves and bark are noted in Table 4.

The International Fragrance Association (IFRA) publishes restrictions for fragrance ingredients. Constituents of *Hamamelis virginiana* (witch hazel) that have restrictions established by the International Fragrance Association Standards are listed in Table 6.

During harvest, *Hamamelis virginiana* (witch hazel) plants can be confused with *Coryllus avellana* (hazelnut).[2] The two plants can be distinguished by anatomical and analytical examination.

UV Absorption

Hamamelis virginiana (Witch Hazel)

In ethanol extracts of dried *Hamamelis virginiana* (witch hazel) plant material (most likely leaves), the light absorbance curves peaked between 250 and 280 nm, depending on the method of extraction.[22] Extracts were conducted by

reperculation and microwave 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 2017, Hamamelis Virginiana (Witch Hazel) Water is reported to be used in 386 formulations (255 in leave-on formulations, 122 in rinse-off formulations, and 9 in formulations that are diluted for the bath; Table 7).[23] Hamamelis Virginiana (Witch Hazel) Extract is reported to be used in 359 formulations (266 in leave-on formulations, 91 in rinse-off formulations, and 2 in formulations that are diluted for the bath) and Hamamelis Virginiana (Witch Hazel) Leaf Extract is reported to be used in 218 formulations (138 in leave-on formulations, 73 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 128 or fewer formulations. The VCRP has entries for "Hamamelis Virginiana Flower Water," which is assumed to be Hamamelis Virginiana (Witch Hazel) Flower Water.

The results of the concentration of use survey conducted by the Council in 2017 indicate Hamamelis Virginiana (Witch Hazel) Extract has the highest reported maximum concentration of use; it is used at up to 86% (in skin fresheners).[24] Hamamelis Virginiana (Witch Hazel) Water 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 5% 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 43 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. Therefore, 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 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 and in formulations that come in contact with mucous membranes. Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract and Hamamelis Virginiana (Witch Hazel) Water are used in formulations that may be ingested (including lipsticks, mouth washes, and breathe fresheners) and in formulations for use on babies.

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 and Hamamelis Virginiana (Witch Hazel) Extract are used in body and hand spray formulations at up to 25.8% and 5%, respectively. 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.[25,26] 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.[27,28] Hamamelis Virginiana (Witch Hazel) Extract and Hamamelis Virginiana (Witch Hazel) Water were reported to be used in face powders at concentrations up to 0.05% and 0.093%, respectively. 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.[29-31]

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%-50% and OTC skin protectant drug products (no limit specified). [21CFR346.18; 21CFR347.12]

Hamamelis virginiana (witch hazel) preparations are commonly used for dermatological conditions, including diaper-related dermatitis; however, clinical studies supporting these uses are generally lacking.[2] In Europe, extracts of *Hamamelis virginiana* (witch hazel) folium and/branches are used in teas/poultices (leaf), liquid and dry extracts (leaf 1:1 or 2 with 30%-60% ethanol; bark 5-7:1 with 30% ethanol, respectively), distillates (1:1.12-2.08 with ethanol), ointments, creams, tinctures (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%-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.[3]

TOXICOKINETIC STUDIES

Dermal Penetration

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 are not absorbed into the blood circulation.[2]

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.[2] No further details were provided.

Mucosal

New Zealand White rabbits (n=2/sex) were administered suppositories containing *Hamamelis virginiana* (witch hazel) ethanol extract (0, 20, 100, or 300 mg/kg).[32] 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 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.

Mucosal

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.[32] 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 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 was assessed weekly. Blood was sampled by cardiac puncture on the last day of the observation period. The rats were killed and necropsied, including the digestive tract. 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 the 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) at 100 mg/kg/day was orally administered to rats for three months. There were no abnormalities reported. No further information was provided.[2]

Chronic Toxicity Studies

No published chronic toxicity studies were discovered and no unpublished data were submitted.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY (DART) STUDIES

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

GENOTOXICITY STUDIES

In Vitro

Hamamelis Virginiana (Witch Hazel) Water (concentration not specified) was not genotoxic in a *Salmonella* mammalian microsome assay (stains TA97, TA98, TA100, and TA1535), with and without metabolic activation.[2]

A sister chromatid exchange (SCE) and a chromosome aberration test were performed on Hamamelis Virginiana (Witch Hazel) Water.[33] The results of both assays were negative at up to 5000 µg/mL, with and without metabolic activation.

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.[2,34] Cultures were exposed to the chemicals for 4 h, and cultured for 2 days before plating in soft agar with or without trifluorothymidine (TFT; 3 µg/mL). The negative control was distilled water; the positive controls were methyl methanesulphonate without metabolic activation and ethyl methanesulphonate with metabolic activation. The test substance was tested at least twice and was not identified as a mutagen.

In Vivo

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

CARCINOGENICITY STUDIES

No published oral or inhalation carcinogenicity studies were discovered and no unpublished data were submitted.

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 no. 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.[35-37] 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.

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 once per week for up to 78 weeks.[38] Saline was the control. The extract was made from wild collected 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 1-2 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 addition 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.

DERMAL IRRITATION AND SENSITIZATION STUDIES

No published irritation or sensitization studies were discovered and no unpublished data were submitted.

OCULAR IRRITATION STUDIES

No published ocular irritation studies were discovered and no unpublished data were submitted.

CLINICAL STUDIES

Retrospective and 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 (n = 78).[2,39] 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). Twelve of 231 subjects experienced

adverse events, which included confusion, head lice, cough/allergic reaction, fungal infection/deterioration, otitis, erythema increased, rhinopharyngitis, burning sensation, super-infection, diaper candidiasis, and obstructive bronchitis. The authors considered only two adverse events as potentially *Hamamelis virginiana* (witch hazel)-related (i.e. erythema and burning sensation), which were resolved by the end of the treatment period.

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).[40] One subject had a positive reaction the *Hamamelis virginiana* (witch hazel) distillate.

Subjects (n=1032) that were in clinics to be patch tested for allergens were administered additional patch tests for ointments that contain botanical extracts, including one that contained *Hamamelis virginiana* (witch hazel) extract (25%).[41] 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," 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 8.

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.[42]

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.[43] There were no reported adverse effects from three O/W emulsions containing *Hamamelis virginiana* (witch hazel) distillates (10% *Hamamelis* ketone) from different suppliers applied to skin damaged by UVB light.[44]

There were no adverse events attributed to a cream containing *Hamamelis virginiana* (witch hazel) distillate (up to 0.00064%) when applied to subjects with moderately severe atopic eczema for 14 days.[45]

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.[46] 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

This is a review of the safety of 8 *Hamamelis virginiana* (witch hazel)-derived ingredients as used in cosmetics. The ingredients in this group are derived from the *Hamamelis virginiana* (witch hazel) plant. According to the *Dictionary*, the 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, depending on the method of extraction.

According to VCRP survey data received in 2017, Hamamelis Virginiana (Witch Hazel) Water is reported to be used in 386 formulations (255 in leave-on formulations, 122 in rinse-off formulations, and 9 in formulations that are diluted for the bath). Hamamelis Virginiana (Witch Hazel) Extract is reported to be used in 359 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 128 or fewer formulations.

The results of the concentration of use survey conducted by the Council in 2017 indicate Hamamelis Virginiana (Witch Hazel) Extract has the highest reported maximum concentration of use; it is used at up to 86% (in skin fresheners). Hamamelis Virginiana (Witch Hazel) Water 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 5% 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 over-the-counter (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.

In an experiment where *Hamamelis virginiana* (witch hazel) ethanol extract was administered to rabbits in a suppository in a single dose, 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 were no hematological effects observed. The NOAEL was > 300 mg/kg.

There were no abnormalities reported when *Hamamelis virginiana* (witch hazel) at 100 mg/kg/day was orally administered to rats for three month.

In an experiment where *Hamamelis virginiana* (witch hazel) ethanol extract was administered to rats in a suppository for 28 days, no rats 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 were no hematological effects observed. The NOAEL was > 300 mg/kg.

Hamamelis Virginiana (Witch Hazel) Water was not genotoxic in SCE, chromosome aberration, and Ames tests. Hamamelis Virginiana (Witch Hazel) Water was not mutagenic to mouse lymphoma cells in a 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.

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. 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 subjects had positive results to the 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 subjects with moderately severe atopic eczema for 14 days.

DATA NEEDS

CIR welcomes the submission of all toxicological data that pertain to these ingredients, especially from dermal exposure and at concentration of use. Chemical and physical properties data are also desirable. The data requested include, but are not limited to:

- Constituent profiles for each of these ingredients
- Chemical and physical properties
- Method of manufacture
- Impurity data
- Dermal penetration
- Chronic dermal toxicity
- Inhalation toxicity
- Dermal irritation and sensitization

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. Chemical and physical properties of *Hamamelis virginiana* (witch hazel)-derived ingredients.

Property	Value	Reference
Hamamelis Virginiana (Witch Hazel) Leaf Water[a]		
Physical Form	Liquid	11,18
Color	Clear	18
	Colorless to slight yellow	11
Odor	Characteristic	18
	Characteristic with slight green note	11
Specific Gravity @ 20°C	0.976-0.982	11,18
@ 25°C	0.979-0.983	11,18
Vapor pressure mmHg@ 20°C	18.75	18
Vapor Density mmHg	1.03	18
Melting Point °C	-8	18
Boiling Point °C	88	18
Water Solubility	Very soluble	18
Hamamelis Virginiana (Witch Hazel) Water[a]		
Physical Form	Liquid	12,15-17,19,20
Color	Clear	12,15-17,19,20
Odor	Characteristic	12,15-17,19,20
	Mild	20
Specific Gravity @ 20°C	0.976-0.982	15-17,19,20
@ 25°C	0.979-0.983	15-17,19,20
Vapor pressure mmHg @ 20°C	18.75	16,17
Vapor Density mmHg	1.03	16,17
Melting Point °C	-8	16,17
Boiling Point °C	88	16,17
Water Solubility g/L	Very soluble	16,17

[a] These values are for Hamamelis Virginiana (Witch Hazel) Leaf Water and Hamamelis Virginiana (Witch Hazel) Water at 84%-85% in grain alcohol or ethanol.

Table 3. Constituents found in the bark and leaves of *Hamamelis virginiana* (witch hazel) plants.[21]

Chemical	Plant Part	Low PPM	High PPM
6-methylheptadien-3,5-dione	Leaf	--	25.0
Acetaldehyde	Leaf	--	160.0
Afzelin	Leaf	--	--
Alcohols	Leaf	--	2000.0
Alpha-Ionone	Leaf	--	175.0
Astragalin	Leaf	--	--
Beta-Ionone	Leaf	--	50.0
Catechin-3-gallate	Bark	--	--
Catechin-tannin	Leaf	--	--
Choline	Leaf	--	2000.0
D-Gallocatchein	Bark	--	--
Ellagitannin	Bark	--	--
EO	Leaf	--	5000.0
Esters	Leaf	--	750.0
Gallic-acid	Leaf	--	54400.0
Gallo-tannin	Leaf	--	--
Hamamelidine	Leaf	--	--
Hamamelin	Bark	--	160000.0
Hamamelin	Leaf	--	70000.0
Hamamelitannin	Leaf	--	80000.0
Hamamelitannin	Bark	10000.0	30000.0
Hamamelose	Leaf	--	--
Isoquercitrin	Leaf	--	--
Kaempferol	Leaf	--	--
L-Epicatechin	Bark	--	--
L-Epigallocatechin	Bark	--	--
Leucocyanidin	Leaf	--	--
Leucodelphinidin	Leaf	--	--
Myricetin	Leaf	--	--
Myricetin-3-glucoside	Leaf	--	--
N-hexen-2-al	Leaf	--	485.0
Phenol	Bark	--	--
Phlobaphene	Bark	--	--
Quercetin	Leaf	--	--
Quercitrin	Leaf	--	--
Quinic acid	Leaf	--	--
Safrole	Leaf	--	10.0
Saponins	Leaf	--	--
Spiraeoside	Leaf	--	--
Tannins	Leaf	10000.0	70000.0

Table 4. 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.[5]

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

Table 4. 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.[5]

Compound	Leaf (%)	Bark (%)
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
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

Table 4. 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.[5]

Compound	Leaf (%)	Bark (%)
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 4. 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.[5]

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 4. 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.[5]

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 4. 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.[5]

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	-
Butylhydroxytoulene[b]	-	0.04
β-ionone	0.08	0.07
Not identified	0.25	-
Not identified	0.26	-
Tribuylphosphate[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 5. Constituents of concern found in *Hamamelis virginiana* (witch hazel)

Constituent	Concern	Reference
Afzelin	Cytotoxic, promoted death of neutraphils	47
Geraniol	Potential dermal sensitizer	7
Linalool	Hydroperoxides are potential dermal sensitizers. Safe at up to 4.3% (20% in a consumer fragrance)	6
Phenol	Toxic by ingestion, inhalation, and dermal absorption. Strong dermal irritant. May induce cardiac arrhythmia and is toxic to the liver and kidneys.	48,49
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	50,51
Safrole	Liver cancer (hepatocellular carcinoma, adenoma) in male mice; liver cancer and other tumors in rats.	52

Table 6. Constituents of *Hamamelis virginiana* (witch hazel) that have IFRA standards.[53]

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 are not to exceed 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 7. Frequency of use according to duration and exposure of *Hamamelis virginiana* (witch hazel)-derived ingredients.[23,24]

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 Water**	
Total/range	**128**	**0.00005-4.3**	**359**	**0.000013-86**	**43[e]**	**NR**	**NR**	**4.1-5**
Duration of use								
Leave-on	90	0.00005-4.3	266	0.00003-86	21	NR	NR	NR
Rinse-off	37	0.00005-0.072	91	0.000013-5	21	NR	NR	4.1-5
Diluted for (bath) use	1	NR	2	0.000013-0.5	1	NR	NR	NR
Exposure type								
Eye area	14	NR	12	0.1-35.8	3	NR	NR	NR
Incidental ingestion	1	NR	NR	35.8	NR	NR	NR	NR
Incidental Inhalation-sprays	23[a];26[b]	0.18[a]	2; 79[a]; 128[b]	0.00003-5; 0.0013-86[a]; 0.01[b]	6[a]; 6[b]	NR	NR	NR
Incidental inhalation-powders	26[b]	0.004-4.3[c]	1; 128[b]	0.05; 0.0001-5[c]; 0.01[b]	6[b]	NR	NR	NR
Dermal contact	122	0.00005-4.3	349	0.000013-86	43	NR	NR	4.1-5
Deodorant (underarm)	2[a]	NR	3[a]	0.0013[d]	NR	NR	NR	NR
Hair-noncoloring	3	NR	7	0.0001-0.3	NR	NR	NR	NR
Hair-coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	2	NR	2	NR	NR	NR	NR	NR
Mucous Membrane	6	NR	13	0.000013-35.8	8	NR	NR	NR
Baby	1	NR	NR	NR	NR	NR	NR	NR

	Hamamelis Virginiana (Witch Hazel) Leaf Extract		**Hamamelis Virginiana (Witch Hazel) Water**	
Total/range	**218**	**0.00018-0.011**	**386**	**0.00008-43**
Duration of use				
Leave-on	138	0.00018-0.011	255	0.00008-43
Rinse-off	73	0.00035-0.01	122	0.00066-33.3
Diluted for (bath) use	7	NR	9	NR
Exposure type				
Eye area	9	NR	21	0.04-6.6
Incidental ingestion	NR	NR	5	0.1
Incidental Inhalation-sprays	1; 44[a]; 65[b]	0.00035[a]	92[a]; 81[b]	0.00008-25.8; 1[a]
Incidental inhalation-powders	1; 65[b]	0.0018-0.011[c]	2[c]; 81[b]	0.093; 0.00066-12.9[c]
Dermal contact	195	0.00018-0.011	354	0.00008-43
Deodorant (underarm)	6[a]	0.00018[d]	14[a]	6[d]
Hair-noncoloring	23	0.00035-0.00042	24	2.5
Hair-coloring	NR	NR	NR	NR
Nail	NR	NR	1	4.3
Mucous Membrane	24	NR	45	0.1-1.5
Baby	NR	NR	4	NR

NR = Not Reported; Total = 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] VCRP lists this ingredient as Hamamelis Virginiana Flower Water.

Table 8. *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 800 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.	[42]
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 800 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.	[43]
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.	[44]
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.	[45]

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

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