Safety Assessment of Equisetum arvense-derived Ingredients as Used in Cosmetics

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All interested persons are provided 60 days from the above date (May 19, 2020) to comment on this safety assessment and to identify additional published data that should be included or provide unpublished data which can be made public and included.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 All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a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 Executive Director, Dr. Bart Heldreth.

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D.; Lisa, A. Peterson, Ph.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Executive Director is Bart Heldreth, Ph.D. This report was prepared by Wilbur Johnson, Jr., M.S., Senior Scientific Analyst.
INTRODUCTION

The safety of the following 5 *Equisetum arvense*-derived ingredients as used in cosmetics is reviewed in this scientific literature review.

- Equisetum Arvense Extract
- Equisetum Arvense Leaf Powder
- Equisetum Arvense Juice
- Equisetum Arvense Powder
- Equisetum Arvense Leaf Extract

According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; Dictionary), the *Equisetum arvense*-derived ingredients are reported to function as skin conditioning agents in cosmetic products (Table 1). Common names for the herb *Equisetum arvense* include horsetail and field horsetail.

The published data in this document were identified by conducting an exhaustive search of the world’s literature. A list of the typical search engines and websites used, sources explored, and endpoints that the Expert Panel for Cosmetic Ingredient Safety (Panel) evaluates, is available on the Cosmetic Ingredient Review (CIR) website (https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; https://www.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data may be provided by the cosmetics industry, as well as by other interested parties. Data on the genus and species name *Equisetum arvense* that were identified in a search of the published literature are also included for use in this safety assessment of *Equisetum arvense*-derived ingredients.

Botanicals, such as *Equisetum arvense* -derived ingredients, may contain hundreds of constituents. However, in this assessment, the potential toxicity of each botanical ingredient as a whole, complex mixture is the focus of the review herein.

Also with botanicals, it is often not known how the substance being tested in a study compares to the cosmetic ingredient. In the report text, if it is known that the material being tested is a cosmetic ingredient, the INCI naming convention is used (i.e., the names of cosmetic ingredients are capitalized, without italics (e.g., Equisetum Arvense Extract)). If it is not known that the test substance is the same as the cosmetic ingredient, the taxonomic naming conventions (i.e. with genus and species name italicized (e.g., an *Equisetum arvense* extract)) is used.

CHEMISTRY

Definition and Plant Identification

The ingredients in this report are related as deriviatives from the same species, *Equisetum arvense*. The definitions and reported functions in cosmetics of these *Equisetum arvense*-derived ingredients are presented in Table 1.

*Equisetum arvense* (horsetail) has been described as a non-flowering weed (a perennial with hollow stems and shoots) that is found throughout parts of Europe, Asia, the Middle East, and North America. *Equisetum arvense* is distributed throughout temperate and arctic areas of the northern hemisphere, growing typically in moist soils. It has also been described as an herbaceous perennial relative of ferns consisting of 2 types of stems, namely, sterile non-reproductive and photosynthetic, and reproductive and non-photosynthetic. The latter, 10 to 25 cm long with brown scale leaves and a 10 to 40 mm long spore cone, emerges in spring and then withers, giving rise to the sterile, photosynthetic stems. These stems persist from summer until the first frost. According to another source, *Equisetum arvense* has aerial stems, branched with regular verticilies (2-23 mm in diameter) and terminal strobile in the branches and in the main stem (10 mm long and 4 mm in diameter).

Physical and Chemicals Properties

*Equisetum Arvense Extract*

*Equisetum arvense* is available as a dried extract in powdered form or as a liquid extract. As the plant dries, silica crystals form in the stems and branches.

Method of Manufacture

The method below is general to the processing of *Equisetum arvense* extracts, and it is unknown if it applies to cosmetic ingredient manufacturing.

*Equisetum Arvense Extract*

A method of manufacture relating to the preparation of three different extracts of *Equisetum arvense* (sterile stems) is available in the published literature. Air dried and powdered plant material (100 g) was macerated with petroleum ether overnight, and afterwards with 70% methanol (24 h). After filtration, the methanolic extract was concentrated to dryness. The dry residue was dissolved in hot water and then separated by liquid-liquid extraction into the chloroform, ethyl acetate, and *n*-butanol extracts.
Composition

The following composition data could be characterized as general information relating to *Equisetum arvense* or *Equisetum arvense* extracts, and it is unknown if it applies to the cosmetic ingredients that are being reviewed in this safety assessment.

Data on flavonoid composition reveal the existence of 2 chemotypes of *Equisetum arvense*, one in Asia and North America, and the other in Europe. According to other sources, acids that have been isolated from *Equisetum arvense* include acetic acid (tricarboxylic acid), ascorbic acid (ketolactone), malic acid (dicarboxylic acid), oxalic acid (dicarboxylic acid), and the following phenolic acids: caffeic acid, cinnamic acids, p-coumaric acid, gallic acid, p-hydroxybenzoic acid, protocatechuic acid, and vanillic acid. Other components include polyenic acids, rare dicarboxylic acids (equisetolic acid), flavonoids, and styrylpyrones.

Additional data on the composition of *Equisetum arvense* indicate that it contains more than 10% inorganic substances (two-thirds of which are silicic acid and potassium salts). Specifically, the aerial parts of *Equisetum arvense* contain flavonoids, saponins, caffeic acid and other phenolic compounds, alkaloids, sterols (β-sitosterol, campesterol, and isoferucosterol), and minerals (primarily silicon and potassium salts). According to other sources, acids that have been isolated from *Equisetum arvense* include acetic acid (tricarboxylic acid), ascorbic acid (ketolactone), malic acid (dicarboxylic acid), oxalic acid (dicarboxylic acid), and the following phenolic acids: caffeic acid, cinnamic acids, p-coumaric acid, gallic acid, p-hydroxybenzoic acid, protocatechuic acid, and vanillic acid. Other components include polyenic acids, rare dicarboxylic acids (equisetolic acid), flavonoids, and styrylpyrones.

The concentration ranges (µg/g) for some essential elements in *Equisetum arvense* have been determined to be: iron (193.4 - 1757.9), manganese (23.6 - 143.7), zinc (15.4 - 32.7), selenium (0.13 - 0.92), and copper (11.3 - 21.8). Among the components (oligo-β-glucans) of the *Equisetum arvense* cell wall are the tetrasaccharide, β-glucosyl-(1→4)-β-glucosyl-(1→4)-β-glucosyl(1→3)-glucose and the trisaccharide, mixed-linkage (1→3, 1→4)-β-D-glucan. The enzyme thiaminase (which breaks down vitamin B1) also occurs in *Equisetum arvense*.10

*Equisetum Arvense Extract*

Whether or not flavonoids or phenolic acids are the predominant compounds in *Equisetum arvense* extracts is dependent upon the extractant that is used. In one publication, flavonoids were the main compounds in ethyl acetate and butanol *Equisetum arvense* extracts, and phenolic acids were the major constituents in the aqueous *Equisetum arvense* extracts. These data are summarized in Table 2. According to another source, the following water-soluble acids have been detected in an aqueous extract of *Equisetum arvense* (whole, air-dried plant): acetic acid, arabinonic acid, citric acid, ferulic acid, fumaric acid, gluconic acid, glyceric acid, malic acid, malonic acid, phosphoric acid, quinic acid, and threonic acid.

Composition data on a methanol extract of *Equisetum arvense* (aerial parts) indicate the presence of 2 phenolic petrosins, namely onitin and onitin-9-O-glucoside, and the following 4 flavonoids: apigenin, luteolin, kaempferol-3-O-glucoside, and quinamercurin-3-O-glucoside. The following % composition values for flavonoid and caffeic acid derivatives of the hydro-alcoholic (20:80, v/v) extract of *Equisetum arvense* stems have been calculated (computed from the high performance liquid chromatography (HPLC) peak areas): quercetin (21.1%), quercetin 3-O-glucoside (49.6%), quercetin 3-O-(6"-O-malonylglucoside) (8.8%), 5-O-caffeoyl shikimic acid (4.4%), monocaaffeoyl meso-tartaric acid (3%), and dicafeoyl meso-tartaric acid (1.6%).

Composition data on *Equisetum arvense* (water and methanol extract) grown in Asia versus *Equisetum arvense* grown in Europe are presented in Table 3. In addition to these data, the researchers presented an accumulation profile (graph) of quercetin glucosides (absolute content, % dry weight) in *Equisetum arvense* during 2 growing seasons which indicated that development of the total amount (% dry weight) of the main flavonoids quercetin 3-O-glucoside and quercetin 3-O-(6"-O-malonylglucoside) was different over several years of observation. An accumulation profile (graph) of quercetin glucosides (proportional content, % total flavonoids) in *Equisetum arvense* during 2 growing seasons indicated that few differences were found in the proportional content (% of flavonoid content) of the 2 main flavonoids in several years of observation. Also, it was found that there was a decrease in quercetin 3-O-(6"-O-malonylglucoside) and a simultaneous increase in quercetin 3-O-glucoside toward the end of the growing period.

Impurities

One source indicates the following mean values for 3 toxic metals in *Equisetum arvense*: lead (14.07 mg/kg), cadmium (0.139 mg/kg), and mercury (0.014 mg/kg). In this analysis, neither the plant parts nor the methods of extraction and testing were stated.

Nicotine has been detected in British species of *Equisetum arvense*. The amount of nicotine obtained from 5 g of dried plant material (British *Equisetum arvense*) has been estimated, using ultraviolet (UV) spectrophotometry, to be not more than 2 mg.
USE

Cosmetic

The safety of *Equisetum arvense* - derived ingredients is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetics 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 cosmetics industry in response to surveys, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.

According to 2020 VCRP data, MoniceArvense Extract is reported to be used in 340 cosmetic products (227 leave-on products, 111 rinse-off products, and 2 products that are diluted for (bath) use; Table 4). Of the *Equisetum arvense* - derived ingredients that are being reviewed in this safety assessment, this is the greatest reported use frequency. The results of a concentration of use survey completed in 2018 and provided by the Council in 2019 indicate that Equisetum Arvense Extract is being used at maximum use concentrations up to 0.4% in leave-on products (body and hand products [not spray]), and at maximum use concentrations up to 0.00078% in rinse-off products (skin cleansing products). Equisetum Arvense Extract is the only *Equisetum arvense* - derived ingredient in this safety assessment for which use concentration data were provided in response to the Council survey. Additionally, according to both VCRP and Council survey data, Equisetum Arvense Juice and Equisetum Arvense Leaf Powder are not reported to be used in cosmetic products.

It should be noted that frequency of use data on *Equisetum arvense* (horsetail) are also included in Table 4. Because neither the plant part(s) associated with the name *Equisetum arvense* nor whether the name corresponds to a plant part extract is stated, it is not possible to specifically associate the frequency of use data on *Equisetum arvense* with any of the 5 *Equisetum arvense* - derived ingredients that are reviewed in this safety assessment.

Cosmetic products containing *Equisetum arvense* - derived ingredients may be applied to the skin/hair, or incidentally, may come in contact with the eyes (e.g., Equisetum Arvense Extract and Equisetum Arvense Leaf Extract). Equisetum Arvense Extract is used in products that come in contact with mucous membranes during product use (e.g., mouth washes and breath fresheners [concentrations up to 0.0002%] and lipsticks [concentrations unknown]); thus, Equisetum Arvense Extract may be incidentally ingested. Products containing *Equisetum arvense* - derived ingredients may be applied as frequently as several times per day and may come in contact with the skin for variable periods following application. Daily or occasional use may extend over many years.

Equisetum Arvense Extract is reported to be used in cologne and toilet waters, and in other fragrance preparations (concentrations unknown). 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 below 10 µm, compared with pump sprays. Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount. Equisetum Arvense Extract is reported to be used in face powders (concentrations unknown). Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.

The *Equisetum arvense* - derived ingredients are not restricted from use in any way under the rules governing cosmetic products in the European Union.

Non-Cosmetic

*Equisetum arvense* (horsetail) is an herbal remedy that dates back to ancient Rome and Greece. Traditionally, it was used to stop bleeding, heal ulcers and wounds, and for the treatment of tuberculosis and kidney problems. The aboveground parts of this plant are used for medicinal purposes. Because *Equisetum arvense* contains silicon, which strengthens bone, some practitioners recommend it as a treatment for osteoporosis (not an FDA-approved use). It is also used as a diuretic, and the diuretic effects of *Equisetum arvense* may enhance the toxic effects of certain medications, such as digoxin (used to treat congestive heart failure), phenytoin (for seizures), anticoagulants, and others. Thus, individuals taking prescription medications should not take *Equisetum arvense* without first consulting a health care provider.

In Japan, *Equisetum arvense* (field horsetail) sporophyte (tsukushi) is consumed as food in sweetened vinegar, cooked food, and chopped fish. Furthermore, in Asian traditional medicine, the aerial parts of *Equisetum arvense* have been used to treat hemorrhage, urethritis, jaundice, and hepatitis. Sterile stems of *Equisetum arvense* are used in herbal medicine in various countries, constituting the “Queseti herba” of European Pharmacopeias. According to another source, *Equisetum arvense* is used mainly for its diuretic properties, and also has the following uses: analgesic, hemostatic, astringent, and treatment for digestive disorders and kidney/bladder stones.

According to the US FDA, *Equisetum arvense* is among the ingredients that have been present in over-the-counter (OTC) drug products for use as a digestive aid (21 CFR 310.545). However, based on evidence currently available, there are inadequate data to establish general recognition of safety and effectiveness of this ingredient for this specified use.
TOXICOKINETIC STUDIES

No relevant toxicokinetic studies on *Equisetum arvense*-derived ingredients were found in the published literature. In general, toxicokinetics data are not expected to be found on botanical ingredients because each botanical ingredient is a complex mixture of constituents.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Oral

A single-dose, oral toxicity study on *Equisetum arvense* was performed using groups of male and female rats (strain and number per group not stated). Doses of 800 mg/kg, 2000 mg/kg, and 5000 mg/kg were administered orally (method not stated). No deaths or abnormal changes in body weight occurred, and no toxicity signs were observed at necropsy. The approximate LD$_{50}$ value was $> 5000$ mg/kg.

Intraperitoneal

The acute toxicity of an *Equisetum arvense* extract (hydroalcoholic extract) was evaluated using groups of 8 male Wistar rats. The groups received intraperitoneal (i.p.) doses of 1000 mg/kg, 2000 mg/kg, and 5000 mg/kg. Control animals were dosed with saline. The number of survivors was recorded on the following day. Mortalities were observed only in the 2000 mg/kg group (12.5% of the animals) and in the 5000 mg/kg group (37.5% of the animals). In all 3 dose groups, transitory respiratory depression and elevated sedation were observed. Both signs persisted to the end of the 240 min observation period, and were dose-dependent.

Short-Term Toxicity Studies

Oral

*Equisetum Arvense Powder*

In a short-term study, male Sprague-Dawley rats (groups of 6) were fed an *Equisetum arvense* powder (0.4% or 4%) in a 20% casein diet, with and without cholesterol (0.5% cholesterol and 0.15% sodium cholate), for 14 days. At a concentration of 0.4% or 4% in either diet, the test material did not influence food intake or growth. There also were no apparent effects on serum liver lipids after feeding with either concentration in both diets. However, on days 9 to 12 of feeding with 4% of an *Equisetum arvense* powder in the cholesterol diet, 4 of 6 rats lost their hair, and dermatitis was observed on the neck, head, nose, and back. At microscopic examination, dense infiltration of neutrophils and lymphocytes was observed in the dermis and subcutaneous tissue. At the center of the eruption, the dermis was ulcerated. The number of mast cells was also increased. These changes at microscopic examination were diagnosed as nonspecific inflammatory lesion of the skin. Reversal of the dermatitis was noted when the diet was changed to commercial pellets. Serum immunoglobulin E (IgE) levels, measured by enzyme-linked immunoassay, indicated that the induction of IgE may not necessarily be involved in the dermatitis caused by *Equisetum arvense* intake. In 2 additional experiments (21 rats total), rats were fed an *Equisetum arvense* powder (concentration not stated) in a cholesterol diet (composition not stated) for 4 weeks and 6 weeks. Six of 21 rats from the 2 experiments had dermatitis on the neck and back. The incidence of dermatitis after feeding for 4 weeks and 6 weeks was approximately 20% and 30%, respectively.

Intraperitoneal

*Equisetum Arvense Extract*

An *Equisetum arvense* extract (dried stem, ethanol and water extract) was administered to 10 male Wistar rats, at a daily i.p. dose of 50 mg/kg for 8 weeks. Signs of toxicity were not observed during the treatment period.

Subchronic Toxicity Studies

Oral

The subchronic oral toxicity of *Equisetum arvense* (powder extracted with hot water; plant part not stated) was evaluated in a study involving groups of 10 male and female F344 rats. The groups were fed *Equisetum arvense* at a concentration of 0.3%, 1%, or 3% in the diet (powdered basal diet) for 13 weeks. Animals of the control group received diet only. Test and control animals were killed at the end of the study, and histopathological examinations of internal organs were performed. Histopathological examination was extended to all tissues of the 0.3% and 1% dietary groups if lesions were frequently found in the 3% dietary group. None of the animals died and no obvious clinical signs were observed in any of the animals during the study. Body weights and cumulative body weight gains in all dietary groups were similar to control values. Additionally, there were no differences in food consumption between the groups. Urinalyses revealed no significant differences in any of the parameters evaluated among the groups. However, the protein levels in males of the 1% and 3% dietary groups were decreased. Additional results are summarized below.

Statistically significant alterations in hematological parameters (e.g., mean corpuscular hemoglobin and platelet count) were observed, but no dose-dependence was apparent. However, a trend toward a dose-dependent decrease in the white
blood cell count was noted in females. There were no statistically significant differences in organ weights. However, a tendency toward a decrease in absolute adrenal weights was observed in males. No treatment-related macroscopic changes were observed at necropsy. However, the following histopathological changes (minimal grade changes) were observed in treated animals: spontaneous inflammatory/proliferative lesions in the liver (3% dietary group, 2 males), spontaneous inflammatory and proliferative lesions in the pancreas (1 female, 3% dietary group), liver microgranulomas (3% dietary group, 1 male and 2 females), kidney atrophy (3 males [0.3% group], 2 males [1% group], and 1 male [3% group]; 1 female [3% group]), and ovarian cysts (3% dietary group, 1 female). Eosinophilic bodies and alpha 2u-globulin expression in the proximal tubules of the kidney were observed in all male rats, including the control group. No treatment-related findings were observed in other tissues and organs of male or female rats. The no-observed-adverse-effect level (NOAEL) for *Equisetum arvense* was determined to be more than 3% in male and female rats (> 1.79 g/kg body weight/day [males]; > 1.85 g/kg body weight/day [females]).

**Chronic Toxicity Studies**

Data on the chronic toxicity of *Equisetum arvense*-derived ingredients reviewed in this safety assessment were neither found in the published literature, nor were these data submitted.

**DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES**

Data on the developmental and reproductive toxicity of the *Equisetum arvense*-derived ingredients reviewed in this safety assessment were neither found in the published literature, nor were these data submitted.

**GENOTOXICITY STUDIES**

**In Vitro**

The genotoxicity potential of *Equisetum arvense* (plant part, method of preparation, and doses not stated) was evaluated in a reverse mutation test using the following bacterial strains: *Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537, and *Escherichia coli* strain WP2uvrA. Details relating to the test protocol were not included. The number of revertant colonies per plate was not increased in any bacterial strain, and *Equisetum arvense* was non-genotoxic in this assay.

A chromosomal aberration test on *Equisetum arvense* (plant part, method of preparation, and doses not stated) was performed using Chinese hamster lung cells. Details relating to the test protocol were not included. However, it was stated that the short treatment method and the continuous treatment method were used. Using both methods, the incidence of cells with chromosomal aberrations was less than 5%. It was concluded that *Equisetum arvense* did not have any potential for inducing chromosomal aberrations.

**Equisetum Arvense Extract**

The acquired micronucleus formation in unirradiated and irradiated samples of human blood lymphocytes cultured with an *Equisetum arvense* extract (ethanol extract of whole, or cut, dried sterile aerial parts; 0.025, 0.05, 0.1, and 0.2 mg/ml) was evaluated using the cytochalasin block micronucleus test. Centromere-positive micronuclei were identified by fluorescence in situ hybridization, using a DNA probe labeled with alpha-satellite digoxigenin. The yield of micronuclei increased in unirradiated samples in a concentration-dependent manner. A reduction in the level of radiation-induced micronuclei in a concentration-dependent manner was also reported. In the control (unirradiated samples), 36.8% of micronuclei were centromere positive (MNC+). In irradiated samples, the percentage of MNC+ ranged from 10.8% to 15.3%. These results were indicative of a clastogenic mechanism for micronuclei formation. The authors noted that this *Equisetum arvense* extract had weak clastogenic properties.

The genotoxicity of an *Equisetum arvense* extract (stem hydro-alcoholic (20:80, v/v) extract) was evaluated in the micronucleus test. Human blood samples were cultured with the extract (62.5 µg/ml) for a total of 67 h. Cell cultures without the extract (also contained cytochalasin B, 6 µg/ml) served as negative controls. Blood samples were also incubated with quercetin (1.3 µg/ml) for comparative purposes. Test results consisted of the number of micronuclei-containing cells per 1000 scored cells and as the incidence of micronuclei formation relative to the incidence of micronuclei formation in the control sample. The incidence (21%, mean of 5 measurements) of micronucleus formation in the sample treated with the extract was higher than that of the control sample. This incidence of micronucleus formation was also comparable to that caused by quercetin alone (20% incidence).

**In Vivo**

*Equisetum arvense* (doses, plant part, and method of derivation not stated) was evaluated for genotoxicity potential in the rat (strain not stated) micronucleus test. Details relating to the test protocol were not included in this publication abstract. The incidence of micronucleated polychromatic erythrocytes (MNPCEs) was not significantly increased, and *Equisetum arvense* was classified as non-genotoxic in this assay.


**CARCINOGENICITY STUDIES**

Data on the carcinogenicity of the *Equisetum arvense*-derived ingredients reviewed in this safety assessment were neither found in the published literature, nor were these data submitted.

**OTHER RELEVANT STUDIES**

**Hepatotoxicity**

The short-term oral toxicity of *Equisetum arvense* (plant part, method of preparation, and dose not stated) was evaluated using Wistar rats (number not stated). Details relating to the test protocol were not included. Repeated oral dosing for 7 days induced the following important changes in hepatic structure: decrease in the number of hepatocytes, increase in the cytoplasmic volume, increase in the production of nuclear volume in hepatic cells, and coagulative necrosis in central areas.

*Equisetum Arvense Extract*

The hepatotoxicity of an *Equisetum arvense* extract (aqueous extract of shade-dried and powdered *Equisetum arvense*) was evaluated using groups of 10 adult male Wistar rats. The animals received graded doses of the extract (30 mg/kg, 50 mg/kg, and 100 mg/kg; 1 dose per group) by gavage for 14 days. The control group was dosed with distilled water. Blood samples were collected (schedule not stated) to determine hepatic enzymes (aspartate amino transferase [AST], alanine amino transferase [ALT], and gamma glutamyl transferase [γ-GT]) seric activities. Hepatic tissue fragments were obtained for histological analysis. None of the animals in either of the 3 dose groups died. Additionally, when compared to the control group, dosing did not change serum activities of hepatic enzymes. Only benign changes in the hepatic morphology were observed in the 3 dose groups as well as in the control group. Centrolobular steatosis and cellular tumefaction (hydropic degeneration) were observed in the 3 dose groups. However, only centrolobular steatosis was observed in the control group. The authors concluded that oral treatment with graded doses of *Equisetum Arvense* Extract was not able to produce significant hepatic changes, when compared to the control group. They also noted that further studies are necessary in order to evaluate the chronic hepatotoxicity of *Equisetum arvense* in rats.

In another study, an *Equisetum arvense* extract (methanol extract) had a hepatoprotective effect in human hepatoma Hep G2 cells incubated with tacrine (hepatotoxin).

**Cytotoxicity**

*Equisetum Arvense Extract*

An *Equisetum arvense* extract (water and ethanol extract) was evaluated for anti-proliferative activity using mouse melanoma B16 cells. This cell line is derived from a spontaneous skin tumor in C57Bl/6 mice. Test concentrations ranged from <0.25 mg/ml to >0.5 mg/ml. After a 2-day incubation period with the extract, cell counts were made with a hemicytometer and cell viability was assessed by trypan blue exclusion. Each test was performed 6 times, and the extract concentration that caused 50% growth inhibition (IC50) was determined. A cytotoxic effect was not observed (i.e., no effect on cell proliferation) at low concentrations (<0.25 mg/ml). This *Equisetum arvense* extract caused a significant (statistically significant not stated) cytotoxic (antiproliferative) effect at high concentrations (>0.5 mg/ml). An IC50 of 1.5 mg/ml was reported for *Equisetum arvense* extract.

The cytotoxicity of an *Equisetum arvense* extract (water extract; drug extract ratio[DER] 1:20) against human leukemia cells (U 937 cells) in vitro was evaluated. Cultures were incubated with the extract at concentrations of 124, 248, and 496 µg dry matter/ml for 48 h. Cytotoxicity was increased in a dose-dependent manner. Whether or not the cell death was due to apoptosis was investigated. Test material concentrations of 124 µg/ml and 248 µg/ml did not influence the apoptotic process. However, the highest concentration of this *Equisetum arvense* extract (496 µg/ml) induced early and late apoptosis, when compared to the control (cells cultured without the extract).

The growth inhibitory activities of several different *Equisetum arvense* extracts (aerial parts; ethyl acetate, chloroform, petroleum ether, n-butanol, and water extracts) were evaluated using 3 histologically different human cancer cell lines (HeLa [human cervix epidermoid tumor cell line], MCF7 [human breast adenocarcinoma cell line], and HT-29 [human colon adenocarcinoma cell line]). The extracts (20 µl per well) were added in order to achieve final concentrations for each extract of 0.0625 to 1 mg/ml. The HeLa human cervix epidermoid tumor cells were found to be the most sensitive to all of the extracts. Ethyl acetate, chloroform, and petroleum ether extracts exhibited a statistically significant (p < 0.01) antiproliferative effect in the HeLa cell line (in 0.125 to 1 mg/ml concentration range), with IC50 values ranging from 0.23 to 0.76 mg/ml. The n-butanol extract did not induce 50% inhibition of HeLa cell growth in the 0.0625 to 1 mg/ml concentration range, but growth inhibition effects at 0.5 to 1 mg/ml were statistically significantly different (p < 0.01) when compared to the control (not stated). Except for the n-butanol extract, all of the extracts statistically significantly decreased MCF-7 cell growth over the entire concentration range. The effects of the ethyl acetate and chloroform extracts were most prominent (p < 0.01) in the 0.125 to 0.5 mg/ml concentration range. However, in this concentration range, no extract caused 50% inhibition of MCF-7 cell growth. Both ethyl acetate and petroleum ether extracts caused a statistically significant (p < 0.01) antiproliferative effect in the HT-29 cell line, with IC50 values ranging from 0.32 to 0.53 mg/ml. Based on the IC50 values, the antiproliferative activity of the extracts decreased in the following order: ethyl acetate > chloroform > petroleum ether.
Morphological changes that resembled necrosis were observed in all cell lines. The most prominent morphological changes were observed in HeLa cells treated with ethyl acetate, chloroform, and n-butanol.

**Equisetum Arvense Leaf Extract**

The ability of an *Equisetum arvense* leaf extract (ethanol extract) to induce apoptosis was studied using A549 lung carcinoma cells.\(^{38}\) The extract was evaluated at concentrations of 100 µg/ml and 150 µg/ml using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) cytotoxicity assay. Acridine orange staining was used to access apoptosis. The development of an orange or orange-red color was indicative of disruption of the cell membrane. Following treatment with both concentrations, the cells were floating (sign of early apoptosis). Additionally, the edges of many cells were not clear and the cytoplasm was not as transparent when compared to untreated control cells. Overall, the cell structure was completely desegregated, with a hard-shelled appearance. Fifty percent of the cells treated with 100 µg/ml developed orange fluorescence. More than 70% of the cells developed orange fluorescence after treatment with 150 µg/ml.

**Effect on Osteoclastogenesis**

An *Equisetum arvense* extract (hydromethanolic extract) was assessed for effects on human osteoclastogenesis using human peripheral blood mononuclear cells (PBMC), as osteoclast precursor cells, and human bone marrow osteoblastic cells (hBMC).\(^{39}\) PBMC cultures and co-cultures of PBMC + hBMC were incubated for 21 days with this extract at concentrations ranging between 0.00016 and 0.5 mg/ml. Control cultures without the extract were maintained. The extract did not affect spontaneous osteoclastogenesis. However, it caused a dose-dependent inhibitory effect (statistically significant at concentrations ≥ 0.004 mg/ml) in osteoclast precursors committed to osteoclastogenesis.

**Antimicrobial Activity**

The in vitro antimicrobial activity of an *Equisetum arvense* extract (stem; hydro-alcoholic (20:80, v/v) extract) against the following bacterial/fungal strains was evaluated: *Staphylococcus aureus*, *Escherichia coli* 95, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Salmonella enteritidis* (all bacterial strains), and the fungal strains *Aspergillus niger* and *Candida albicans*.\(^{12}\) Disks containing the extract (5 µg per disk) and a bacterial strain were incubated for 24 h. The incubation period for plates containing a fungal strain and the extract (5 µg per disk) was 48 h. For each disk, the diameter (mm) of the inhibition zone was measured. Disks containing ampicillin and nystatin (30 µg per disk) served as positive controls, and disks containing methanol served as negative controls. *Staphylococcus aureus* was found to be the strain that was most resistant to this extract. The most sensitive strain was *Pseudomonas aeruginosa*. Results indicated that the antimicrobial activity of this extract (5 µg per disk) was comparable to the antimicrobial activity of the positive controls (30 µg per disk).

**DERMAL IRRITATION AND SENSITIZATION STUDIES**

Data on the dermal irritation and sensitization potential of the *Equisetum arvense*-derived ingredients reviewed in this safety assessment were neither found in the published literature, nor were these data submitted.

**OCULAR IRRITATION STUDIES**

Data on the ocular irritation potential of the *Equisetum arvense*-derived ingredients reviewed in this safety assessment were neither found in the published literature, nor were these data submitted.

**CLINICAL STUDIES**

**Case Reports**

A dermatitis patient was regularly in contact with *Equisetum arvense* (plant part(s) not stated) in the proximity of his house.\(^{15}\) In the hour after exposure, he developed dermatitis (resembled seborrheic dermatitis) of the right hand and face after passive inhalation of tobacco smoke. Additionally, a fresh exposure to *Equisetum arvense* induced a more rapid reaction, which necessitated local application of epinephrine and oral antihistamines. The authors noted that this patient’s history of atopic reactions with nicotine as a hapten in tobacco smoke correlated with the possible presence of nicotine in *Equisetum arvense*. It was also noted that nicotine has been detected in British species of *Equisetum arvense*.

A woman with no history of atopy developed rhinoconjunctivitis symptoms (dyspnea and general malaise) and contact dermatitis after inhaling steam while cooking green beans, potatoes, and carrots.\(^{40}\) The patient also used *Equisetum arvense* to lose weight. Prick test results for *Equisetum arvense* (1/1 (w/v) concentration in isotonic saline solution) were positive; the same was true for celery and carrots. Conjunctival challenge with *Equisetum arvense* (1/10 dilution) also yielded a positive response. Additionally, conjunctival challenge with celery (1/10 dilution) and carrot (1/1000 dilution) yielded positive responses. The authors noted that *Equisetum arvense* contains a protein that is similar to a protein that is found in carrots.
Hair loss and fragile nails were observed in a male consumer who took *Equisetum arvense* (3 units/day) for 12 months.\(^{31}\) It was noted that the hair loss could have been associated with the reported effect of *Equisetum arvense* in reducing the bioavailability of thiamine after chronic consumption.

Another case report involves a woman with a history of arterial hypertension, dyslipidemia, and bilateral adrenalectomy due to macronodular bilateral hypertrophy of the adrenal glands.\(^{42}\) Additionally, over a period of 9 years, the patient had recurrent episodes of mild acute pancreatitis. A drug-induced origin of the pancreatitis, secondary to a chronic overproduction of endogenous steroids and hormone replacement treatment with corticosteroids, was suspected. Modification of the treatment regimen resulted in normal laboratory test values. However, at 6 months after treatment modification, the patient was diagnosed with mild acute pancreatitis. At that time, the patient admitted habitual consumption of *Equisetum arvense* infusions. At 14 months after suspension of the *Equisetum arvense* (plant part, method of preparation, and dose not stated) infusions, the patient remained asymptomatic. The authors concluded that the episode of pancreatitis was triggered by *Equisetum arvense* infusions.

*Equisetum Arvense Extract*

Hand and facial swelling were observed in a female patient after 2 days of oral consumption of an herbal diuretic containing an *Equisetum arvense* extract (ethanol extract).\(^{11}\) The diuretic was taken 3 times daily and consisted of 225 mg of *Equisetum arvense* dry extract (DER 7.5-10.5:1; extraction solvent = ethanol (70% v/v)). Recovery was noted after treatment of symptoms.

**SUMMARY**

The safety of 5 *Equisetum arvense*-derived ingredients as used in cosmetics is reviewed in this safety assessment. *Equisetum arvense* (horsetail) has been described as a non-flowering weed that is found throughout parts of Europe, Asia, the Middle East, and North America.

Data on flavonoid composition reveal the existence of 2 chemotypes of *Equisetum arvense*, one in Asia and North America, and the other in Europe. *Equisetum arvense* from Asia and North America contains luteolin-5-O-glucoside and its malonyl ester, but these compounds are not found in *Equisetum arvense* from Europe. The dominant compounds in *Equisetum arvense* from Europe are quercetin 3-O-glucoside, apigenin 5-O-glucoside, and dicaffeoyl-meso-tartaric acid. Di-E-caffeoyl-meso-tartaric acid is a marker for both chemotypes. Whether or not flavonoids or phenolic acids are the predominant compounds in *Equisetum arvense* extracts is dependent upon the extractant that is used.

The preparation of different extracts of *Equisetum arvense* has been described. Air dried and powdered plant material was macerated with petroleum ether overnight, and afterwards with 70% methanol. After filtration, the methanolic extract was concentrated to dryness. The dry residue was dissolved in hot water and then separated by liquid-liquid extraction into the chloroform, ethyl acetate, and n-butanol extracts.

According to 2020 VCRP data, Equisetum Arvense Extract is reported to be used in 340 cosmetic products (227 leave-on products, 111 rinse-off products, and 2 products that are diluted for (bath) use). Of the *Equisetum arvense*-derived ingredients that are being reviewed in this safety assessment, this is the greatest reported use frequency. The results of a concentration of use survey submitted by the Council in 2019 indicate that Equisetum Arvense Extract is being used at maximum use concentrations up to 0.4% in leave-on products (body and hand products [not spray]), and at maximum use concentrations up to 0.00078% in rinse-off products (skin cleansing products). Equisetum Arvense Extract is the only *Equisetum arvense*-derived ingredient in this safety assessment for which use concentration data were provided in response to the Council survey. According to VCRP and Council survey data, Equisetum Arvense Juice and Equisetum Arvense Leaf Powder are not being used in cosmetic products.

In Asian traditional medicine, the aerial parts of *Equisetum arvense* have been used to treat hemorrhage, urethritis, jaundice, and hepatitis. According to the FDA, *Equisetum arvense* is among the ingredients that have been present in over-the-counter (OTC) drug products for use as a digestive aid. However, based on evidence currently available, there are inadequate data to establish general recognition of safety and effectiveness of this ingredient for this specified use.

A single-dose, oral toxicity study on *Equisetum arvense* was performed using groups of male and female rats (strain and number per group not stated). The approximate LD\textsubscript{50} value was > 5000 mg/kg. None of the animals died and there were no signs of toxicity at necropsy.

An *Equisetum arvense* extract (hydroalcoholic extract) was evaluated for acute toxicity using groups of 8 male Wistar rats. The groups received i.p. doses of 1000 mg/kg, 2000 mg/kg, and 5000 mg/kg. Mortalities were observed only in the 2000 mg/kg group (12.5% of the animals) and in the 5000 mg/kg group (37.5% of the animals). Transitory respiratory depression and elevated sedation (dose-dependent) were observed in all 3 dose groups.

In a short-term study, male Sprague-Dawley rats (groups of 6) were fed an *Equisetum arvense* powder (0.4% or 4%) in a 20% casein diet with and without cholesterol (0.5% cholesterol and 0.15% sodium cholate) for 14 days. At a concentration of 0.4% or 4% in either diet, *Equisetum arvense* powder did not influence food intake or growth, or have an effect on serum liver lipids. However, on days 9 to 12 of feeding with 4% *Equisetum arvense* powder in the cholesterol diet, 4 of 6 rats lost their hair and dermatitis was observed on the neck, head, nose, and back. At microscopic examination, these changes were
were not observed. In 2 additional experiments, rats were fed an *Equisetum arvense* powder (concentration not stated) in a cholesterol diet (composition not stated) for 4 weeks and 6 weeks. Six of 21 rats from the 2 experiments had dermatitis on the neck and back. The incidence of dermatitis after feeding for 4 weeks and 6 weeks was approximately 20% and 30%, respectively.

An *Equisetum arvense* extract (dried stem, ethanol and water extract) was administered to 10 male Wistar rats, at a daily i.p. dose of 50 mg/kg for 8 weeks. Signs of toxicity were not observed.

The subchronic oral toxicity of *Equisetum arvense* (powder extracted with hot water; plant part not stated) was evaluated in a study involving groups of 10 male and female F344 rats fed *Equisetum arvense* at a concentration of 0.3%, 1%, or 3% in the diet (no further information on test substance composition or plant part(s) included) for 13 weeks. None of the animals died, and no obvious clinical signs were observed in any of the animals during the study. Statistically significant alterations in hematological parameters (e.g., mean corpuscular hemoglobin and platelet count) were observed, but no dose dependence was apparent. Histopathological changes were observed in the liver, pancreas, kidneys, and ovaries. The NOAEL for *Equisetum arvense* was determined to be more than 3% in male and female rats (> 1.79 g/kg body weight/day [males]; > 1.85 g/kg body weight/day [females]).

*Equisetum arvense* (plant part, method of preparation, and doses not stated) was evaluated in a reverse mutation test using *S. typhimurium* strains TA98, TA100, TA1535, and TA1537, and *E. coli* strain WP2uvrA. Results were negative. A chromosomal aberration test on *Equisetum arvense* (plant part, method of preparation, and doses not stated) was performed using Chinese hamster lung cells. It was concluded that *Equisetum arvense* did not have any potential for inducing chromosomal aberrations. The acquired micronucleus formation in unirradiated and irradiated samples of human blood lymphocytes cultured with *Equisetum arvense* extract (ethanol extract, 0.025, 0.05, 0.1, and 0.2 mg/ml) was evaluated using the cytchalasin block micronucleus test in vitro. *Equisetum arvense* extract (ethanol extract) had weak clastogenic properties in this test. The genotoxicity of an *Equisetum arvense* extract (stem hydro-alcoholic (20:80, v/v) extract) was evaluated in another in vitro micronucleus test. Human blood samples were cultured with the extract (62.5 µg/ml). The incidence (21%, mean of 5 measurements) of micronucleus formation in the sample treated with the extract was higher than that of the control sample.

*Equisetum arvense* (plant part, method of preparation, and doses not stated) was evaluated for genotoxicity potential in the rat (strain not stated) micronucleus test in vivo. The incidence of MNPCEs was not significantly increased, and *Equisetum arvense* was classified as non-genotoxic in this assay.

The hepatotoxicity of an *Equisetum arvense* extract (aqueous extract of shade-dried and powdered *Equisetum arvense*) was evaluated using groups of 10 adult male Wistar rats. The animals received graded doses of the extract (30 mg/kg, 50 mg/kg, and 100 mg/kg; 1 dose per group) by gavage for 14 days. None of the animals died, and significant hepatic changes were not observed.

An *Equisetum arvense* extract (water and ethanol extract) caused a significant (statistical significance not stated) cytotoxic (antiproliferative) effect in mouse melanoma B16 cells at high concentrations (> 0.5 mg/ml). An IC$_{50}$ of 1.5 mg/ml was reported. The cytotoxicity of an *Equisetum arvense* extract (water extract; DER 1:20) against human leukemia cells (U 937 cells) in vitro was evaluated. Concentrations of 124 µg/ml and 248 µg/ml did not influence the apoptotic process. However, the highest concentration of *Equisetum arvense* extract (496 µg/ml) induced early and late apoptosis, when compared to the control (cells cultured without *Equisetum arvense* extract). The growth inhibitory activity of *Equisetum arvense* extracts (aerial parts; ethyl acetate, chloroform, and petroleum ether, n-butanol, and water extracts) was evaluated using 3 histologically different human cancer cell lines (HeLa, MCF7, and HT-29 cells). The HeLa human cervix epidermoid tumor cells were found to be the most sensitive to all of the extracts. Ethyl acetate, chloroform, and petroleum ether extracts exhibited a statistically significant (p < 0.01) antiapoptotic effect in the HeLa cell line (in 0.125 to 1 mg/ml concentration range), with IC$_{50}$ values ranging from 0.23 to 0.76 mg/ml.

The ability of an *Equisetum arvense* leaf extract (ethanol extract) to induce apoptosis was studied using A549 lung carcinoma cells. The extract was evaluated at concentrations of 100 µg/ml and 150 µg/ml using the MTT cytotoxicity assay. *Equisetum arvense* leaf extract manifested cytotoxicity and decreased the cell viability of A549 cells in a concentration-dependent manner.

An *Equisetum arvense* extract (hydromethanolic extract) was assessed for effects on human osteoclastogenesis using human PBMCs, as osteoclast precursor cells, and hBMCs. PBMC cultures and co-cultures of PBMC + hBMC were incubated for 21 days with *Equisetum arvense* extract at concentrations ranging between 0.00016 and 0.5 mg/ml. The hydromethanolic extract caused a dose-dependent inhibitory effect (statistically significant at concentrations $\geq 0.004$ mg/ml) in osteoclast precursors committed to osteoclastogenesis (stimulated or co-cultured with osteoblasts).

The in vitro antimicrobial activity of an *Equisetum arvense* extract (stem hydro-alcoholic (20:80, v/v) extract) against *Staphylococcus aureus*, *Escherichia coli* 95, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Salmonella enteritis* (all bacterial strains), and the fungal strains *Aspergillus niger* and *Candida albicans* was evaluated. Results indicated that the
antimicrobial activity of *Equisetum arvense* extract (5 µg per disk) was comparable to the antimicrobial activity of the positive controls (ampicillin and nystatine, 30 µg per disk).

Hand and facial swelling were observed in a female patient after 2 days of oral consumption of an herbal diuretic containing an *Equisetum arvense* extract (225 mg of *Equisetum arvense* dry extract (DER 7.5-10.5:1; extraction solvent = ethanol (70% v/v)). A dermatitis patient who was regularly in contact with *Equisetum arvense* developed dermatitis of the right hand and face after passive inhalation of tobacco smoke; a fresh exposure to *Equisetum arvense* induced a more rapid reaction. A female patient with rhinoconjunctivitis and contact dermatitis had inhaled steam while cooking vegetables and also consumed *Equisetum arvense* for weight loss. Prick test results for *Equisetum arvense* (1/1 (w/v) concentration in isotonic saline solution) were positive. Conjunctival challenge with *Equisetum arvense* (1/10 dilution) also yielded a positive response. Hair loss and fragile nails were observed in a male consumer who took *Equisetum arvense* (3 units/day) for 12 months. Mild acute pancreatitis was observed in a female patient who admitted to habitual consumption of *Equisetum arvense* infusions. The patient remained asymptomatic after suspension of the *Equisetum arvense* infusions.

A double-blind clinical trial was performed using 108 women who had given birth for the first time. Fifty-four women were treated with a 3% *Equisetum arvense* sterile ointment (hydroalcoholic solvents containing ethanol), and another group of 54 women was treated with a placebo. The ointment was applied by 54 women twice per day (12 ± 2 h intervals) for 10 days. Skin problems (not defined) were observed in 11 subjects. In another double-blind clinical trial (randomized), 12 healthy male subjects were administered a standardized dried extract (extractant not stated) of *Equisetum arvense* (aerial parts) consisting of 0.026% total flavonoids, at a dose of 900 mg/day. Two other groups of male subjects (12 male subjects [received corn starch placebo, 900 mg/day]; 12 male subjects [received hydrochlorothiazide, 25 mg/day]) were also included. The groups were subjected to a 3-step treatment protocol in which the order of the 3 treatments (Equisetum Arvense Extract, hydrochlorothiazide, and placebo) was alternated. Each treatment was administered for 4 consecutive days at each stage, and there was a 10-day washout interval between treatment stages. Dosing with the extract produced a diuretic effect, and rare minor adverse events (e.g., headache) were reported. Overall, the dosing regimen was well-tolerated.

**INFORMATION SOUGHT**

The CIR is seeking the following information on all the *Equisetum arvense*-derived ingredients for use in the resulting safety assessment:

- chemical characterization and method of production data, specific to use in cosmetic formulations;
- dermal toxicity data; and
- skin irritation and sensitization data at maximum reported use concentrations
**Table 1. Definitions and Functions of the Ingredients in this Safety Assessment.**

<table>
<thead>
<tr>
<th>Ingredient/CAS No.</th>
<th>Definition &amp; Structures</th>
<th>Function(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Equisetum Arvense Extract 71011-23-9</td>
<td>Equisetum Arvense Extract is the extract of the whole herb, <em>Equisetum arvense</em>.</td>
<td>Skin-Conditioning Agents - Miscellaneous</td>
</tr>
<tr>
<td>Equisetum Arvense Juice 71011-23-9 (generic)</td>
<td>Equisetum Arvense Juice is the juice expressed from <em>Equisetum arvense</em>.</td>
<td>Skin-Conditioning Agents - Miscellaneous</td>
</tr>
<tr>
<td>Equisetum Arvense Leaf Extract 71011-23-9</td>
<td>Equisetum Arvense Leaf Extract is the extract of the leaves of <em>Equisetum arvense</em>.</td>
<td>Skin-Conditioning Agents - Miscellaneous</td>
</tr>
<tr>
<td>Equisetum Arvense Leaf Powder</td>
<td>Equisetum Arvense Leaf Powder is the powder obtained from the dried, ground leaves of <em>Equisetum arvense</em>.</td>
<td>Skin-Conditioning Agents - Miscellaneous</td>
</tr>
<tr>
<td>Equisetum Arvense Powder</td>
<td>Equisetum Arvense Powder is the powder obtained from the dried, ground whole plant, <em>Equisetum arvense</em>.</td>
<td>Skin-Conditioning Agents - Humectant</td>
</tr>
</tbody>
</table>

**Table 2. Dominant Compounds in *Equisetum arvense* extracts, based on solvent.**

<table>
<thead>
<tr>
<th>Phenolic Compounds</th>
<th>Quantity (mg/g dry extract) in Ethyl Acetate Extract</th>
<th>Quantity (mg/g dry extract) in n-Butanol Extract</th>
<th>Quantity (mg/g dry extract) in Aqueous Extract</th>
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<tbody>
<tr>
<td>Isoquercitrin</td>
<td>152</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Apigenin 6-O-glucoside</td>
<td>27.40</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Apigenin 3-O-glucoside</td>
<td>26.20</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>di-E-caffeoyl-meso-tartaric acid</td>
<td>---</td>
<td>100</td>
<td>10</td>
</tr>
<tr>
<td>Phenolic Acid 1 (unnamed)</td>
<td>---</td>
<td>---</td>
<td>3</td>
</tr>
<tr>
<td>Phenolic Acid 2 (unnamed)</td>
<td>---</td>
<td>---</td>
<td>6</td>
</tr>
</tbody>
</table>

**Table 3. Composition Data on Equisetum Arvense Extract from Asia and Europe.**

<table>
<thead>
<tr>
<th>Components</th>
<th><em>Equisetum arvense</em> (methanol and water extract) from Asia</th>
<th><em>Equisetum arvense</em> (methanol and water extract) from Europe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apigenin 4'-O-glucoside</td>
<td>Detected (quantity not stated)</td>
<td>Detected (quantity not stated)</td>
</tr>
<tr>
<td>Apigenin 5-O(6'-O-malonylglicoside)</td>
<td>Detected (quantity not stated)</td>
<td>Detected (quantity not stated)</td>
</tr>
<tr>
<td>Apigenin 5-O-glucoside</td>
<td>&gt;500 µg/g dry weight</td>
<td>&gt;500 µg/g dry weight</td>
</tr>
<tr>
<td>5-O-Caffeoylshikimic acid</td>
<td>Detected (quantity not stated)</td>
<td>Detected (quantity not stated)</td>
</tr>
<tr>
<td>Chlorogenic acid</td>
<td>Detected (quantity not stated)</td>
<td>Detected (quantity not stated)</td>
</tr>
<tr>
<td>Dicaffeoyl-meso-tartaric acid</td>
<td>&gt;500 µg/g dry weight</td>
<td>&gt;500 µg/g dry weight</td>
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<tr>
<td>Equisetumpyone</td>
<td>Detected in fertile sprouts only</td>
<td>Detected in fertile sprouts only (quantity not stated)</td>
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<tr>
<td>Genkwanin 4'-O-glucoside</td>
<td>Detected (quantity not stated)</td>
<td>Detected (quantity not stated)</td>
</tr>
<tr>
<td>Genkwanin 5-O-glucoside</td>
<td>Detected (quantity not stated)</td>
<td>Detected (quantity not stated)</td>
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<tr>
<td>Genkwanin 5-O(6'-O-malonylglicoside)</td>
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<td>Detected (quantity not stated)</td>
</tr>
<tr>
<td>Gossypetin 7-O-glucoside</td>
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<td>Detected in fertile sprouts only (quantity not stated)</td>
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<td>Kaempferol 3-O-glucoside</td>
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<tr>
<td>Kaempferol 3-O-sophoroside</td>
<td>Detected (quantity not stated)</td>
<td>Detected (quantity not stated)</td>
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<tr>
<td>Kaempferol 3-O(6'-O-malonylglicoside)</td>
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<td>Detected (quantity not stated)</td>
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<tr>
<td>Kaempferol 3-O(6'-O-malonylglicoside)-7-O-glucoside</td>
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<td>Detected (quantity not stated)</td>
</tr>
<tr>
<td>Kaempferol 3,7-O-diglucoside</td>
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<td>Detected (quantity not stated)</td>
</tr>
<tr>
<td>Luteolin 5-O-glucoside</td>
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<td>Not detected</td>
</tr>
<tr>
<td>Luteolin 5-O(6'-O-malonylglicoside)</td>
<td>Detected (quantity not stated)</td>
<td>Not detected</td>
</tr>
<tr>
<td>Monocaffeoyl-meso-tartaric acid</td>
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<td>Detected (quantity not stated)</td>
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<tr>
<td>Protoapoquinin 4'-O-glucoside</td>
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<td>Protogenkwanin 4'-O-glucoside</td>
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<td>Detected in fertile sprouts only (quantity not stated)</td>
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<td>Quercetin 3-O-glucoside</td>
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<td>&gt;500 µg/g dry weight</td>
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<td>Quercetin 3-O-sophoroside</td>
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<td>&gt;500 µg/g dry weight</td>
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<td>Quercetin 3-O(6'-O-malonylglicoside)</td>
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<td>Detected (quantity not stated)</td>
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<td>Quercetin 3,7-O-diglucoside</td>
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<td>Detected (quantity not stated)</td>
</tr>
<tr>
<td></td>
<td>Equisetum Arvense Extract</td>
<td>Equisetum Arvense Leaf Extract</td>
</tr>
<tr>
<td>---------------------</td>
<td>---------------------------</td>
<td>--------------------------------</td>
</tr>
<tr>
<td></td>
<td># of Uses</td>
<td>Conc. (%)</td>
</tr>
<tr>
<td>Totals*</td>
<td>340</td>
<td>0.0000011-0.4</td>
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<tr>
<td><strong>Duration of Use</strong></td>
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<tr>
<td>Leave-On</td>
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<td>0.01-0.4</td>
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<tr>
<td>Rinse off</td>
<td>111</td>
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</tr>
<tr>
<td>Diluted for (bath) Use</td>
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<td>NR</td>
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<tr>
<td><strong>Exposure Type</strong></td>
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<td></td>
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<td>Eye Area</td>
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<td>NR</td>
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<tr>
<td>Incidental Ingestion</td>
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<td>0.0002</td>
</tr>
<tr>
<td>Incidental Inhalation - Sprays</td>
<td>3; 50-110*</td>
<td>0.0002*</td>
</tr>
<tr>
<td>Incidental Inhalation - Powders</td>
<td>3;110*</td>
<td>0.01-0.4*</td>
</tr>
<tr>
<td>Dermal Contact</td>
<td>250</td>
<td>0.00078-0.4</td>
</tr>
<tr>
<td>Deodorant (underarm)</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Hair - Non-Coloring</td>
<td>84</td>
<td>0.0000011-0.0006</td>
</tr>
<tr>
<td>Hair - Coloring</td>
<td>3</td>
<td>NR</td>
</tr>
<tr>
<td>Nail</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Mucous Membrane</td>
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<tr>
<td>Baby Products</td>
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<td>NR</td>
</tr>
<tr>
<td><strong>Totals/Conc. Range</strong></td>
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<td>NR</td>
</tr>
<tr>
<td><strong>Exposure Type</strong></td>
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<tr>
<td>Eye Area</td>
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</tr>
<tr>
<td>Incidental Ingestion</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Incidental Inhalation - Sprays</td>
<td>3-4*</td>
<td>NR</td>
</tr>
<tr>
<td>Incidental Inhalation - Powders</td>
<td>4*</td>
<td>NR</td>
</tr>
<tr>
<td>Dermal Contact</td>
<td>14</td>
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<tr>
<td>Deodorant (underarm)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Hair - Non-Coloring</td>
<td>6</td>
<td>NR</td>
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<tr>
<td>Hair - Coloring</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Nail</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Mucous Membrane</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Baby Products</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

* NS = Not Surveyed
* Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.
**Not an International Nomenclature Cosmetic Ingredient (INCI) name, but uses under this name are in the VCRP
aIt is possible that these products may be sprays, but it is not specified whether the reported uses are sprays
bIt is possible that these products may be powders, but it is not specified whether the reported uses are powders
cNot specified that these products are sprays or powders, but it is possible the use can be as a spray or powder, therefore the information is captured in both categories

d**equisetum arvense** (horsetail)**


