Safety Assessment of Plant-Derived Charcoal Ingredients as Used in Cosmetics

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The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Thomas J. Slaga, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D., and the Senior Director is Monice Fiume. This safety assessment was prepared by Christina L. Burnett, M.S., Senior Scientific Analyst/Writer, CIR.

1620 L Street, NW, Suite 1200 ◇ Washington, DC 20036-4702 ◇ ph 202.331.0651
cirinfo@cir-safety.org

ABBREVIATIONS

C-fix	carbon content
CIR	Cosmetic Ingredient Review
Council	Personal Care Products Council
CPSC	Consumer Product Safety Commission
D_{50}	size distribution for 50% of particles
DART	developmental and reproductive toxicity
Dictionary	web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI)
DMSO	dimethyl sulfoxide
EC_3	effective concentration inducing a stimulation index of 3
ECHA	European Chemicals Agency
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
FDA	Food and Drug Administration
HET-CAM	hen's egg test-chorioallantoic membrane
INC	International Nomenclature Committee
LLNA	local lymph node assay
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
NOAEL	no-observable-adverse-effect level
NR	not reported
OECD	Organisation for Economic Co-Operation and Development
OTC	over-the-counter
Panel	Expert Panel for Cosmetic Ingredient Safety
SI	stimulation index
TG	test guideline
US	United States
VCRP	Voluntary Cosmetic Registration Program
WHO	World Health Organization

ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of Charcoal, Charcoal Extract, and Charcoal Powder (including activated charcoal), all of which are reported to function as opacifying agents and two of which are reported to function as abrasives and absorbents in cosmetic products. The Panel reviewed the available data to determine the safety of these ingredients. The Panel concluded that these 3 plant-derived charcoal ingredients are safe in cosmetics in the present practices of use and concentration described in this safety assessment.

INTRODUCTION

This assessment reviews the safety of Charcoal, Charcoal Extract, and Charcoal Powder (including activated charcoal) as used in cosmetic formulations. These ingredients, as used in cosmetics, are all carbonaceous materials produced by the pyrolysis of plant-derived organic matter. Only plant-derived charcoal ingredients are included in this assessment; accordingly, charcoal derived from petroleum or other mineral sources are excluded from this review.

According to the *Dictionary*, all three ingredients are reported to function in cosmetics as opacifying agents (Table 1).[1] Charcoal is also reported to function as a deodorant agent, both Charcoal and Charcoal Powder as abrasives and absorbents, and Charcoal Extract as a skin-conditioning agent – miscellaneous in cosmetics. Additionally, Charcoal Powder is reported to function as a colorant; however, Charcoal Powder is not listed as an approved colorant by the United States (US) Food and Drug Administration (FDA) and therefore not allowed to be used as such in cosmetics in the US. Additionally, colorants (with the exclusion of so called "coal tar exemption" hair dyes) are not under the purview of the Panel and use as such is not addressed in this assessment.

The International Nomenclature Committee (INC) has determined that activated charcoal is a synonym for Charcoal Powder, and is listed as such in the *Dictionary*.[1] However, because activated charcoal is the more commonly known name in published literature and the medical community, it will be referred to as such herein in the appropriate studies but categorized under the ingredient heading Charcoal Powder.

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an extensive search of the world's literature; the search was last conducted October 2023. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that the Panel typically evaluates, is provided 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 are provided by the cosmetics industry, as well as by other interested parties.

Much of the data included in this safety assessment was found on the European Chemicals Agency (ECHA) website.[2] Please note that the ECHA website provides summaries of information generated by industry, and it is those summary data that are reported in this safety assessment when ECHA is cited.

CHEMISTRY

Definition

The definitions of the charcoal ingredients included in this review are provided in Table 1.[1] Charcoal is the dried, carbonaceous material obtained from the heating of organic substances, and Charcoal Extract and Charcoal Powder are the extract and the dried powder, respectively, of Charcoal. The INC has determined that activated charcoal is a synonym for Charcoal Powder.[1]

Chemical Properties

Available chemical properties for activated charcoal and Charcoal are summarized in Table 2. Charcoal has low water solubility.[2] In 3 samples of Charcoal with carbon content (C-fix) ranging from 73.3% to 88.7%, particle size distribution smaller than 100 µm was reported in 0.53 - 0.87% of samples tested, and only < 0.3% of the particles of the samples tested were smaller than 10 µm. Activated charcoal is insoluble in water and in organic solvents.[3,4]

Charcoal ingredients adsorb chemicals and substances from air and water, with the activation of charcoal increasing material volume, breaking turbo-static carbon structures that form surface functional groups, and removing non-crystallized carbons.[5] Surface area-to-mass ratios and van der Waals force contribute to adsorption properties of these ingredients.

Method of Manufacture

The following methods of manufacturing are general to the production of charcoal ingredients, and it is unknown whether these methods are used in the manufacture of charcoal ingredients for use in cosmetics.

Charcoal

Charcoal sourced from bamboo is manufactured by cutting bamboo into small pieces, washing through boiling in distilled water, and then drying at nearly 110°C to remove moisture.[5] The bamboo is then carbonized in an oven at 800 - 1200°C for several hours. Lower temperatures may be utilized to produce different quality charcoals. From here, the charcoal may undergo activation to increase adsorption properties.

Charcoal Powder

According to *the Food Chemicals Codex*, activated charcoal is prepared by carbonizing and activating organic substances, which may include sawdust, peat, lignite, coal, cellulose residues, coconut shells, and petroleum coke.[3] However, cosmetic charcoal ingredients are manufactured from plant-derived products only, such as bamboo. The raw materials may be carbonized and activated at a high temperature with or without the addition of inorganic salts in a stream of activating gases such as steam or carbon dioxide. Alternatively, the raw material may be treated with a chemical-activating agent such as phosphoric acid or zinc chloride, with the mixture then carbonized at an elevated temperature followed by removal of the chemical-activating agent by water washing.

Activated charcoal sourced from bamboo (see above) is produced by mixing the bamboo charcoal with carbon dioxide, nitric acid, ammonia, or other materials (not specified) before it is heated to 500 - 1200°C for several hours.[5] The annealed bamboo charcoal is then cooled.

Composition and Impurities

Charcoal Powder

According to the *Food Chemicals Codex*, activated charcoal may not contain more than 3 mg/kg arsenic, 10 mg/kg lead, or 0.004% heavy metals (as lead).[3] Testing specifications were also provided for organic impurities such as cyanogen compounds and higher aromatic hydrocarbons, but quantifiable limits were not described.

USE

Cosmetic

The safety of the cosmetic ingredients addressed in this assessment is evaluated based on data received from the US FDA and the cosmetics industry on the expected use of these ingredients in cosmetics and does not cover their use in airbrush delivery systems. Data are submitted by the cosmetic industry via the US FDA Voluntary Cosmetic Registration Program (VCRP) database (frequency of use) and in response to a survey conducted by the Personal Care Products Council (Council) (maximum use concentrations). The data are provided by cosmetic product categories, based on 21CFR Part 720. For most cosmetic product categories, 21CFR Part 720 does not indicate type of application and, therefore, airbrush application is not considered. Airbrush delivery systems are within the purview of the US Consumer Product Safety Commission (CPSC), while ingredients, as used in airbrush delivery systems, are within the jurisdiction of the FDA. Airbrush delivery system use for cosmetic application has not been evaluated by the CPSC, nor has the use of cosmetic ingredients in airbrush technology been evaluated by the FDA. Moreover, no consumer habits and practices data or particle size data are publicly available to evaluate the exposure associated with this use type, thereby preempting the ability to evaluate risk or safety.

Use for Charcoal Powder and activated charcoal has been reported separately to both the VCRP and in the concentration of use survey conducted by the Council, and accordingly, are presented separately in this safety assessment. According to 2023 VCRP survey data, Charcoal Powder has the highest frequency of use; it is reported to be used in 231 formulations, with a majority of uses in rinse-off formulations, such as skin cleansing preparations (Table 3).[6] Activated charcoal is reported to be used in 53 formulations, also with the majority of uses in rinse-off formulations. The results of the concentration of use survey conducted by the Council in 2021 indicate that Charcoal Powder has the highest concentration of use; it is used at up to 4.8% in eyeliners and at up to 4% in paste masks (mud packs).[7]

Some charcoal ingredients may be incidentally ingested or used near the eye or mucous membranes. For example, Charcoal Powder is reported to be used in lipstick (0.25%), eyeliners (4.8%), and bath soaps and detergents (3%).[7] Additionally, some of the ingredients are used in cosmetic sprays and could possibly be inhaled; for example, Charcoal Powder is reported to be used in a hair spray at 0.001%.[7] It has been noted that Charcoal Powder may be used in dry shampoos; although the VCRP and Council survey data do not specify use in dry shampoos, Charcoal Powder is reported to be used in 24 shampoo formulations at a maximum use concentration of 0.03%. Please refer to the Panel's respiratory exposure resource document for information regarding exposures from incidental inhalation (https://www.cir-safety.org/cir-findings).

Although products containing some of these ingredients may be marketed for use with airbrush delivery systems, this information is not available from the VCRP or the Council survey. Without information regarding the frequency and concentrations of use of these ingredients (and without consumer habits and practices data or particle size data related to this use technology), the data are insufficient to evaluate the exposure resulting from cosmetics applied via airbrush delivery systems.

The charcoal ingredients named in the report are not restricted from use in any way under the rules governing cosmetic products in the European Union (EU).[8]

Non-Cosmetic

Charcoal has been used since ancient Egyptian times, initially for metallurgy and cooking.[9,10] The first recorded use in oral hygiene was reported by Hippocrates in ancient Greece.[9,11] Medicinal use to treat the ingestion of poisons was first reported in the early 1800s.[9,10]

Charcoal (non-activated) has been studied as a treatment for irritable bowel syndrome,[12] and in tattoo localization in surgical procedures (peat-derived).[13] Wood charcoal has been present in over-the-counter (OTC) digestive aids; however, there are inadequate data to establish general recognition of the safety and effectiveness of this ingredient for the specified use (21CFR Part 310.545). Nano charcoal (derived from bamboo) has been studied as a drug delivery carrier.[14,15] Charcoal (derived from bamboo) also has been studied for use in water treatment to adsorb heavy metals, such as cadmium,[16] and fluorinated compounds, such as perfluorooctanoic acid.[17] Charcoal is also reported to be used in the filters of some types of cigarettes.[18] Charcoal has been reported to be a food ingredient in China, Taiwan, South Korea, and Japan.[19]

Per the *Food Chemicals Codex*, activated charcoal functions as a decolorizing agent, a taste- and odor-removing agent, and a purification agent in food processing.[3] The FDA allows the use of activated charcoal for purification in the production of synthetic paraffin that is used in direct and indirective food additives (21CFR Part 172.250 and Part 172.615). Activated charcoal has been present in OTC digestive aids and antidiarrheal drug products; however, there are inadequate data to establish general recognition of the safety and effectiveness of this ingredient for the specified uses (21CFR Part 310.545). The FDA lists activated charcoal as beneficial in the treatment of aspirin overdose, but only after emesis and lavage, and if less than 3 h has passed since ingestion (21CFR Part 343.80). Activated charcoal is used in emergency medicine and veterinary medicine as an oral and hemoperfusion adsorbent of ingested poisons.[20-28] The World Health Organization (WHO) has listed activated charcoal as an essential medicine for its use as an antidote used in poisonings.[29] Dressings and treatments using up to 98% activated charcoal have been studied for use in controlling foul odor associated with severe skin disorders and chronic wounds.[30,31] Activated charcoal has also been studied for use in tattoo localization in surgical procedures,[32] in topical drug-delivery systems,[33] as a treatment for intrahepatic cholestasis of pregnancy,[34] as a treatment for high cholesterol,[35] and as a treatment for uremia in patients with renal disease.[10,36]

TOXICOKINETIC STUDIES

No toxicokinetic studies were reported for charcoal ingredients in the published literature and unpublished data were not submitted. However, a summary of toxicity data under "Basic Toxicokinetics" in the ECHA dossier for Charcoal concluded that there is low potential for absorption by oral ingestion and dermal application.[2]

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Oral

Charcoal Powder

An acute oral study of Charcoal Powder (bamboo-sourced) was performed in accordance with Organisation for Economic Co-Operation and Development (OECD) test guideline (TG) 420.[37] Groups of 10 male and 10 female Sprague-Dawley rats received a single dose by gavage of 11,240 mg/kg bw of one of 2 kinds of Charcoal Powder with either 93.5% purity (size distribution of 50% of particles (D_{50}) = 2.175 µm) or 95.5% purity (D_{50} = 10.514 µm) in ultrapure deionized water. Control groups received only the vehicle. Mortality and clinical signs of toxicity were assessed at 30 min, 4 h, and daily up to 14 d post-treatment, and body weights were recorded on observation days 1, 7, and 14. The animals were killed at the end of the observation period, and organs were analyzed. No mortalities were observed. All rats exposed to Charcoal Powder had black colored feces, which resolved after 2 d. One rat given the Charcoal Powder with 93% purity had diarrhea, which abated after 2 d. No other clinical signs were observed. No significant differences were found in the body weights in the groups treated with either Charcoal Powder when compared to the controls. No treatment-related histological changes in the organs were observed. The LD_{50} of both types of Charcoal Powder in both male and female rats was greater than 11,240 mg/kg bw.

Inhalation

Charcoal

In an acute inhalation study performed in accordance with OECD TG 403, 5 male and 5 female Wistar Crl:(WI) BR rats were exposed to a mean concentration of 4.97 mg/l air of Charcoal (carbon content (C-fix) = 80.5%; the test article was micronized powder milled to 150 µm).[2] During testing, 52.3% of the particles generated in the chamber were < 4 µm (considered the respirable fraction); the mass median aerodynamic diameter/geometric standard deviation was 3.523 µm/2.46 µm. The rats were exposed nose-only for 4 h, and then observed for 14 d. No mortality occurred during the exposure period. Clinical signs, specifically decreased activity, general reactions, and dyspnea, were observed between the third hour of inhalation exposure and the first hour of the observation period in both males and females. All animals were symptom-free starting day 1 of the observation period. No toxicologically-relevant findings were noted at necropsy. The LC_{50} was greater than 4.97 mg/l.

Short-Term Toxicity Studies

Oral

Charcoal Powder

In a short-term oral study performed in accordance with OECD TG 407, groups of 5 male and 5 female Sprague Dawley rats received 1 of 2 kinds of Charcoal Powder (93.5% purity; D_{50} = 2.175 µm or 95.5% purity; D_{50} = 10.514 µm) in ultrapure deionized water daily for 28 d via gavage.[37] The Charcoal Powder was sourced from bamboo. The dose levels for both types of Charcoal Powder were 2810, 5620, or 11,240 mg/kg bw. Control groups received only the vehicle. Mortality and clinical signs of toxicity were assessed daily. Feed consumption was recorded once per week. Surviving animals were killed at the end of the treatment period following an 18 h fast. Blood samples and organs were analyzed.

No mortalities or obvious signs of toxicity were observed in the rats in any dose group. A dose-related change in the color of the feces was observed, with increased doses producing darker colored feces. No significant changes were observed in body weight gains or feed consumption. No significant differences were noted in relative weights of the organs or hematological and biochemical parameters of the treated animals when compared to the controls. In the treated rats, the gastrointestinal tract content was black. No other treatment-related macroscopic findings were observed. There were no treatment-related microscopic findings. The no-observed-adverse-effect level (NOAEL) was greater than 11,240 mg/kg bw/d for both Charcoal Powder types in both sexes.[37]

Subchronic Toxicity Studies

Oral

Charcoal Powder

In a 90-d study performed in accordance with OECD TG 408 by the same research group, Charcoal Powder (bamboo-sourced; 93.5% pure; D_{50} = 2.175 µm) was administered orally to groups of 10 male and 10 female Sprague Dawley rats at 0, 2810, 5620, or 11,240 mg/kg bw/d.[19] The test material was mixed in ultrapure water and administered via gavage (2 ml/kg bw). The rats were observed for clinical signs of toxicity, and feed consumption, body and organ weights, and hematological and biochemical parameters were measured. Additional satellite groups (5 males and 5 females each) from the control group and the high dose group were observed for a 28-d recovery period. At the end of the treatment and recovery periods, the rats were killed, blood samples were collected, and the brain, thymus, heart, liver, kidneys, adrenal gland, spleen, testes, epididymides, uterus, and ovaries were weighed. Macroscopic and microscopic examinations were performed.

No mortalities were observed during the dosing period or the recovery period. No clinical signs of toxicity were observed other than a dose-related change in the color of feces in the treated groups, which returned to normal color in the recovery group. No significant differences ($p > 0.05$) were observed in feed consumption or organ weights among the rats in the treatment and recovery periods. All treated rats gained weight normally during the dosing and recovery periods. No significant differences were observed in hematology parameters or other biochemical parameters of the treated rats compared to the controls. After 90 d of treatment, the gastrointestinal tracts of the treated rats were black. No other macroscopic findings were reported at necropsy. Slight inflammatory cell infiltration in the bronchium and cardiac muscles of 5% of the male rats was observed without intergroup differences, and hepatic steatosis, mineralization of the kidney medulla, and eosinophilic granulocyte infiltration of the uterus were observed in 8% of female rats, without difference in severity among all groups. These microscopic findings were not considered treatment-related in any of these rats. The NOAEL was determined to be 11,240 mg/kg bw/d in both sexes.[19]

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY (DART) STUDIES

DART studies for charcoal ingredients were not found in the published literature, and unpublished data were not submitted.

GENOTOXICITY STUDIES

In vitro and in vivo genotoxicity data on Charcoal and Charcoal Powder are summarized in Table 4. Charcoal (C-fix 73.3 to 88.7%) and Charcoal Powder were not mutagenic in Ames tests at up to 5000 µg/plate.[2,19] No clastogenic activity was observed in chromosome aberration tests with V79 Chinese hamster lung cells or human peripheral blood lymphocytes exposed to Charcoal (C-fix 75.75 to 83.3%; up to 5000 µg/ml).[2] No genotoxicity was observed to Charcoal in gene mutation assays with mouse lymphoma cells (C-fix 80.5%; tested up to 2400 µg/ml) or in an in vitro micronucleus test with human peripheral blood lymphocytes (C-fix 83.3%; up to 2000 µg/ml). No mutagenicity was reported in a Comet assay or an erythrocyte micronucleus study of Charcoal Powder (up to 11,240 mg/kg orally) conducted in mice.[19]

CARCINOGENICITY STUDIES

Charcoal Powder

In lung tumor induction studies, Charcoal Powder was given to male C57BL/6 andC3H/He mice with and without the carcinogen 3,4-benzopyrene.[38] Groups of mice (number not reported) received intratracheally 1.0 mg benzopyrene with 0.5 mg of Charcoal Powder or 0.5 mg of benzopyrene with 0.5 mg Charcoal Powder in 0.025 ml of 0.9% sodium chloride

solution once a week for 4, 8, or 16 wk. Control mice (34 for strain C57Bl/6 and 33 for strain C3H/H3) received 0.5 mg of Charcoal Powder in 0.025 ml of 0.9% sodium chloride solution once a week for 8 wk. The mice were examined daily and weighed weekly during the observation period of 120 wk. Animals that died naturally or were killed for humane reasons prior to study end were necropsied. Lungs with trachea and mediastinal organs, liver, spleen, kidneys, adrenals and stomach were examined. For histological examination of early changes of the epithelium of the respiratory tract, 5 mice were killed sequentially 1, 3, 5, 7, and 10 wk after receiving 8 high doses of benzopyrene.

During the study, some of the control mice died of pneumonia without tumors. The mean body weights of the animals that received just Charcoal Powder were observed to increase up until week 30 of the observation period before gradually decreasing until study end. In macroscopic observations, Charcoal Powder was observed to be distributed almost equally in each lobe of the lung after a single instillation of benzopyrene and Charcoal Powder. In the mice that received 8 doses of the high dose of benzopyrene, many tiny nodular lesions were observed on the surface of the lung as early as 2 wk after the last instillation: these lesions were always surrounded by charcoal deposits. In microscopic findings, sections of stained lung showed Charcoal Powder evenly distributed in the periphery of the lung along with the benzopyrene, especially in the terminal bronchioles and alveoli. Occasionally the Charcoal Powder was phagocytosed by alveolar macrophages. In the animals that received both benzopyrene and Charcoal Powder, tumors of various sizes were observed after week 10, with some being highly keratinized squamous cell carcinomas. In the controls (those just receiving Charcoal Powder in solution), no tumors were observed in the C57BL/6 mice within 110 wk and only 1 alveolar-type adenoma was observed in C3H/He mice within 100 wk.[38]

OTHER RELEVANT STUDIES

Cytotoxicity

Charcoal Powder

The effects of highly-porous activated charcoal (coconut-shell sourced; 1 μm) on cell viability was studied in an 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay on human corneal epithelial cells, human foreskin fibroblasts, vaginal epithelial cells, and HeLa cell lines.[33] Activated charcoal was tested at up to 10 mg/ml for 24 h. At the end of incubation, MTT (0.5 mg/ml in whole media) was added and incubated for an additional 3 h. Cell viability was greater than 75% in all cell types. It was concluded that highly porous activated charcoal was not cytotoxic.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Dermal irritation and sensitization data on Charcoal are summarized in Table 5. Charcoal (C-fix 73.3, 80.5, and 88.7%) was not predicted to be irritating in reconstructed human epidermis model tests, nor was it irritating in a rabbit primary skin irritation test when tested under occlusion at a concentration of 100%.[2] In 3 different local lymph node assays (LLNAs) in mice with up to 10% Charcoal (C-fix 73.3, 80.5, and 88.7%), an effective concentration inducing a stimulation index of ≥ 3 (EC_3) was not observed, indicating the lack of dermal sensitization.

OCULAR IRRITATION STUDIES

Ocular irritation data on Charcoal are summarized in Table 6. Charcoal (C-fix 73.3, 80.5, and 88.7%) was not predicted to be an ocular irritant when tested neat in hen's egg test-chorioallantoic membrane (HET-CAM) studies, nor was Charcoal (C-fix 80.5%) irritating in rabbit eyes according to EU criteria when instilled undiluted; slight to severe conjunctival irritant effects that were observed were fully reversible within 1 wk.[2]

CLINICAL STUDIES

Case Report

A 52-yr-old woman presented with intermittent mild loose stool with no other specific medical comorbidities.[39] A colonoscopy revealed numerous small and medium-sized irregular grayish black pigmentations mostly on the background of geographic light grayish discolored mucosa and some on the normal-looking mucosa on the terminal ileum. Microscopic examination of the biopsy specimen taken from the pigmented mucosa showed black, coarse, and dust-like particles with irregular borders freely dispersed or focally aggregated in the lamina propria and submucosa. A review of the patient's medication history after endoscopy revealed she had ingested Charcoal Powder (approximately 10 g) with a glass of water daily for 2 yr. A colonoscopy 5 yr prior revealed no melanosis of the terminal ileum at that time. The pigmented particles were considered exogenous, and the pigmentation was likely due to the Charcoal Powder. The patient was advised to stop ingesting Charcoal Powder. A follow-up colonoscopy 10 mo later found no significant change to the pigmentation of the terminal ileum.

Other Clinical Reports

Charcoal

In a study with irritable bowel syndrome patients, Charcoal (non-activated) in a formulation and as a control was evaluated in 284 patients.[12] The patients orally received at minimum 180 mg Charcoal daily for 12 wk. Endpoints monitored

were overall well-being, decrease in irritable bowel syndrome severity score, other irritable bowel syndrome characteristics, self-assessed gastrointestinal events (e.g., abdominal pain, bloating, stool, etc.), safety/tolerability, and number of patients withdrawn for treatment failure. Mild or moderate adverse events, which mainly affected the gastrointestinal tract, were reported in 21% of the patients that received the formulation and 17% that received the control. No serious, unusual, or unexpected adverse events were observed.

In another study, 26 patients with chronic stasis leg ulcers and 13 patients with suppurating post-operative wounds received a single layer of Charcoal cloth (50 - 800 cm^2).[40] Treatment sites were monitored for wound odor, wound healing, and wound cleansing. No adverse effects to the material were observed.

Charcoal Powder

Several studies have been conducted to investigate whitening, remineralization, and anti-caries claims in dentifrice and mouthwash products.[11,41-49] In one double-blind clinical trial for remineralization and anti-caries effects with 12 subjects using a toothpaste containing activated charcoal (concentration not reported) twice daily for 90 d, no adverse events or side effects were reported or observed.[42]

Activated charcoal was given orally (6 g/d for 8 wk) to 11 stable hemodialysis patients with idiopathic generalized pruritus.[50] Self-assessed itching intensity was recorded by the patients, and changes in skin lesions and serum chemistry, including lipids, alkaline phosphatase, phosphorus, and calcium, were examined during the study. No adverse effects from activated charcoal were noted.

In an efficacy study of an inhaled asthma drug, activated charcoal (suspension; 50 g in 250 ml tap water) was given orally to 33 healthy subjects to prevent gastrointestinal absorption of the test drug.[51] The subjects received the activated charcoal as a 10 g dose prior to inhalation of the test drug and as a 30 g dose during the 1.5 h after inhalation or oral ingestion of the test drug in 4 different treatment scenarios (4 single treatments total). The subjects rinsed their mouths with 2 x 25 ml of activated charcoal-water suspension and with 25 ml tap water prior to swallowing the activated charcoal suspension and water. This rinsing procedure was performed immediately before and after drug administration and repeated after 45 min and 1.5 h. No further details were provided on the dosing of activated charcoal. The efficacy of the activated charcoal was determined via venous blood samples measuring the concentration of the asthma drug. Thirty subjects completed the study; one subject withdrew due to an adverse event (stomatitis; no further details). The most frequently reported adverse events were headache and respiratory tract infection; the adverse events were not specifically attributed to use of activated charcoal.

SUMMARY

The safety of 3 plant-derived charcoal ingredients as used in cosmetics is assessed herein; only plant-derived charcoal ingredients, and not those derived from petroleum or other mineral sources, are included in this assessment. According to the *Dictionary*, all three ingredients are reported to function in cosmetics as opacifying agents and two are reported to function as abrasives and absorbents. Additional functions are reported for each as well; specifically, Charcoal Powder is reported to function as a colorant in cosmetics. However, Charcoal Powder is not listed as an approved colorant by the US FDA and therefore not allowed to be used as such in cosmetics in the US. Furthermore, colorants (with the exception of coal tar hair dyes) are not under the purview of the Panel and use as such in not addressed in this assessment. Per the INC, activated charcoal is a synonym of Charcoal Powder; however, because activated charcoal is the more commonly known name in published literature and the medical community, it will also be referred to as such herein in the appropriate studies but described under the ingredient heading Charcoal Powder.

According to 2023 VCRP survey data, Charcoal Powder has the highest frequency of use; it is reported to be used in 231 formulations, with a majority of uses in rinse-off formulations, such as skin cleansing preparations. Activated charcoal (reported separately from Charcoal Powder even though these 2 names are synonyms) is reported to be used in 53 formulations, also with the majority of uses in rinse-off formulations. The results of the concentration of use survey conducted by the Council in 2021 indicate that Charcoal Powder has the highest concentration of use; it is used at up to 4.8% in eyeliners and up to 4% in paste masks (mud packs).

Charcoal has been used since ancient Egyptian times, initially for metallurgy and cooking. Charcoal ingredients have been studied for many medical treatments, are used as food ingredients in several Asian countries, and are used in filtration. Activated charcoal is used in purification of paraffin used in direct and indirect food additives and is well known for its use in emergency medicine for poisoning treatment.

In an acute oral study, the LD_{50} for Charcoal Powder in male and female rats is greater than 11,240 mg/kg bw. The LC_{50} in an acute rat inhalation study of Charcoal (C-fix 80.5%; 52.3% of particles < 4 μm; mass median diameter/geometric standard deviation = 3.523 μm/2.46 μm) was greater than 4.97 mg/l. The NOAEL for Charcoal Powder in an oral 28-d and 90-d study in rats was 11,240 mg/kg bw/d, which was the maximum dose tested in both studies.

Charcoal (C-fix 73.3 to 88.7%) and Charcoal Powder were not mutagenic in Ames tests at up to 5000 μg/plate. No clastogenic activity was observed in chromosome aberration tests with V79 Chinese hamster lung cells or human peripheral blood lymphocytes exposed to Charcoal (C-fix 75.75 to 83.3%; up to 5 mg/ml). No genotoxicity was observed to Charcoal

(C-fix 80.5%) in gene mutation assays with mouse lymphoma cells (tested up to 2400 µg/ml) or in a cell micronucleus test (C-fix 83.3%) with human peripheral blood lymphocytes (up to 2000 µg/ml). No mutagenicity was reported in a Comet assay and an erythrocyte micronucleus study of Charcoal Powder (up to 11,240 mg/kg orally) conducted in mice.

In a lung tumor induction study using two strains of mice, controls received Charcoal Powder only. No tumors were observed in the C57BL/6 strain of mice during a 110-wk observation period, and only one alveolar-type adenoma was observed in C3H/He mice during a 100-wk observation period.

The cytotoxicity of a highly-porous activated charcoal was studied in an MTT assay on human corneal epithelial cells, human foreskin fibroblasts, vaginal epithelial cells, and HeLa cell lines. Activated charcoal was not cytotoxic in any of the cells.

Charcoal (C-fix 73.3, 80.5, and 88.7%) was predicted to be not irritating in reconstructed human epidermis model tests and was not irritating in a rabbit primary skin irritation test when tested at a concentration of 100%. Charcoal was not sensitizing in 3 different mouse LLNAs at up to 10% (C-fix 73.3, 80.5, and 88.7%). In ocular irritation studies, Charcoal (C-fix 73.3 to 88.7%) was not predicted to be an ocular irritant when tested neat in HET-CAM studies, and it was not irritating in rabbit eyes according to EU criteria.

Clinical studies have been conducted using charcoal ingredients. A clinical study was performed with a toothpaste containing activated charcoal, in which 12 subjects used the test material twice daily for 90 d. No adverse events or side effects were reported or observed. No adverse effects were reported with charcoal ingredients when used as treatments for irritable bowel syndrome, leg ulcers, and idiopathic generalized pruritus. Although adverse events were observed in a study of an inhaled drug comprising in part activated charcoal, to prevent gastrointestinal absorption, those events were not considered attributable to the activated charcoal.

DISCUSSION

The Panel reviewed the safety of 3 plant-derived charcoal ingredients and concluded that these ingredients are safe as used in cosmetics in the present practices of use and concentration described in this safety assessment. The charcoal ingredients reviewed in this safety assessment are derived from plant sources (e.g. bamboo); accordingly, charcoal derived from petroleum and other mineral sources are excluded from this safety assessment.

The Panel concluded that the available data are sufficent for determining the safety of these ingredients for use in cosmetic products. They noted the lack of systemic toxicity in acute and repeated-dose studies at up to 11,240 mg/kg bw and the safe use of activated charcoal (synonymous with Charcoal Powder) as an oral treatment for poisioning. The Panel also noted negative results in irritation and sensitization in tests of dermal exposure, and in genotoxicity using in vitro and in vivo test systems. The lack of developmental and reproductive toxicity data was mitigated by low absorption through oral and dermal routes.

Furthermore, the Panel discussed the issue of incidental inhalation exposure that may result from the use of formulations containing these ingredients (i.e., Charcoal Powder is used in a hair spray at 0.001%). Data available from inhalation studies, including an acute rat study with Charcoal and an intratracheal rat carcinogenicity study with Charcoal Powder, suggest little potential for respiratory effects at doses relevant to cosmetic use. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at https://www.cir-safety.org/cir-findings.

The Panel's respiratory exposure resource document (see link above) notes that airbrush technology presents a potential safety concern, and that no data are available for consumer habits and practices thereof. As a result of deficiencies in these critical data needs, the safety of cosmetic ingredients applied by airbrush delivery systems cannot be assessed by the Panel. Therefore, the Panel has found the data insufficient to support the safe use of cosmetic ingredients applied via an airbrush delivery system.

CONCLUSION

The Expert Panel for Cosmetic Ingredient Safety concluded that the following 3 plant-derived charcoal ingredients are safe in cosmetics in the present practice of use and concentration described in this safety assessment:

Charcoal
Charcoal Extract
Charcoal Powder

Tables

Table 1. Definitions and reported functions of the ingredients in this safety assessment.[1,3]

Ingredient & CAS No.	Definition	Function(s)
Charcoal 16291-96-6	Charcoal is the dried, carbonaceous material obtained from the heating of organic substances.	abrasive; absorbent; deodorant agent; opacifying agent
Charcoal Extract	Charcoal Extract is the extract of Charcoal.	opacifying agent; skin-conditioning agent – miscellaneous
Charcoal Powder 7440-44-0; 64365-11-3; 16291-96-6	Charcoal Powder is finely ground Charcoal. *The chemical name, "activated charcoal" is considered to be a synonym for Charcoal Powder.*	abrasive; absorbent; colorant; opacifying agent

Table 2. Chemical properties.

Property	Value	Reference
Charcoal Powder (reported as activated charcoal)		
Physical Form	black powder or granules	4
Density (g/ml @ 25 ºC)	1.8 - 2.1	52
Melting Point (ºC)	3550	52
Vapor Pressure (mm Hg @ 25 ºC)	0.750	52
Water Solubility	insoluble	2
Organic Solvent Solubility	insoluble	2
Charcoal		
Physical Form	black, porous solid, coarse granules or powder	2
Specific Gravity (@ 20 ºC)	1.41 - 1.50	2
Particle Size Distribution (%) < 100 µm < 10 µm	 0.53 – 0.87 < 0.3	2
Melting Point (ºC)	> 300	2
log K_{ow} (@ 20 ºC)	1.474	2
Water Solubility	low	2

Table 3. Frequency (2023)[6] and concentration (2021)[7] of use according to likely duration and exposure and by product category.

	Charcoal†		Charcoal Extract		Charcoal Powder		activated charcoal	
	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
Totals*	**9**	**NR**	**15**	**0.0004-0.5**	**231**	**0.0001-4.8**	**53**	**0.2-0.5**
summarized by likely duration and exposure**								
Duration of Use								
Leave-On	*3*	*NR*	*3*	*0.0004-0.0038*	*71*	*0.001-4.8*	*11*	*0.2*
Rinse-Off	*6*	*NR*	*12*	*0.0004-0.5*	*157*	*0.0001-4*	*38*	*0.35-0.5*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*3*	*0.005*	*4*	*NR*
Exposure Type*								
Eye Area	NR	NR	NR	NR	3	4.8	1	NR
Incidental Ingestion	NR	NR	NR	NR	28	0.13-0.25	9	NR
Incidental Inhalation-Spray	1[b]	NR	1[a]; 2[b]	0.0004[a]	1; 10[a]; 36[b]	0.001	1[a]; 2[b]	NR
Incidental Inhalation-Powder	1[b]	NR	2[b]	0.0019-0.0038[c]	36[b]	0.0028[c]	2[b]	NR
Dermal Contact	9	NR	10	0.0004-0.5	163	00.001-4.8	44	0.2-0.5
Deodorant (underarm)	NR	NR	NR	NR	2[a]	0.0062	NR	NR
Hair - Non-Coloring	NR	NR	5	0.0004-0.005	38	0.0001-0.7	NR	NR
Hair-Coloring	NR	NR	NR	NR	1	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	4	0.0004-0.5	58	0.001-3	21	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR
as reported by product category								
Bath Preparations (diluted for use)								
Bath Oils, Tablets, and Salts					1	0.001-0.005	3	NR
Other Bath Preparations					2	NR	1	NR
Eye Makeup Preparations								
Eyeliner					NR	4.8		
Mascara					1	NR		
Other Eye Makeup Preparations					2	NR	1	NR
Hair Preparations (non-coloring)								
Hair Conditioner			3	0.0019-0.005	9	0.0005-0.7		
Hair Spray (aerosol fixatives)					1	0.001		
Rinses (non-coloring)			1	NR	1	NR		
Shampoos (non-coloring)			1	0.0004-0.002	24	0.0001-0.03		
Tonics, Dressings, and Other Hair Grooming Aids					1	NR		
Other Hair Preparations					2	NR		
Hair Coloring Preparations								
Hair Bleaches					1	NR		
Makeup Preparations								
Lipstick					NR	0.25		
Makeup Bases					1	NR		
Oral Hygiene Products								
Dentifrices					22	0.13	8	NR
Mouthwashes and Breath Fresheners					2	NR		
Other Oral Hygiene Products					4	NR	1	NR
Personal Cleanliness Products								
Bath Soaps and Detergents			4	0.0019-0.5	20	0.005-3	7	NR
Deodorants (underarm)					2	0.0062		
Other Personal Cleanliness Products			NR	0.0004	7	NR	1	NR
Shaving Preparations								
Shaving Cream					1	0.005		
Other Shaving Preparations			NR	0.0006				

Table 3. Frequency (2023)[6] and concentration (2021)[7] of use according to likely duration and exposure and by product category.

	Charcoal†		Charcoal Extract		Charcoal Powder		activated charcoal	
	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
Skin Care Preparations								
Cleansing	3	NR	2	0.0038-0.05	45	0.0063-0.1	15	0.35
Face and Neck (exc shave)	1	NR	2	0.0038	32	0.0028	2	NR
Body and Hand (exc shave)			NR	0.0019	4	NR		
Moisturizing			1	NR	1	NR	1	NR
Night					4	NR		
Paste Masks (mud packs)	3	NR	1	NR	21	0.037-4	6	0.5
Skin Fresheners			NR	0.0004	2	NR		
Other Skin Care Preparations	2	NR			18	0.01-0.3	7	0.2

†Listed as Bamboo Charcoal in the VCRP database.
NR – not reported
*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.
**Likely duration and exposure is derived based on product category (see Use Categorization https://www.cir-safety.org/cir-findings)
[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.
[b] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories
[c] It is possible these products are powders, but it is not specified whether the reported uses are powders.

Table 4. Genotoxicity studies.

Test Article	Concentration/Dose	Vehicle	Test System	Procedure	Results	Reference
			IN VITRO			
Charcoal (batch with C-fix = 73.3%)	50 - 5000 µg/plate with plate incorporation method; 313 - 5000 µg/plate with pre-incubation method	ethanol	*Salmonella typhimurium* TA97a, TA98, TA100, TA102, and TA1335	Bacterial reverse mutation assay, with and without S9 metabolic activation; in accordance with OECD TG 471; positive and negative controls used	Not mutagenic, with or without metabolic activation, in all tester strains	[2]
Charcoal (batch with C-fix = 80.5%)	50 - 5000 µg/plate with plate incorporation method; 313 - 5000 µg/plate with pre-incubation method	ethanol	*S. typhimurium* TA97a, TA98, TA100, TA102, and TA1335	Bacterial reverse mutation assay, with and without S9 metabolic activation; in accordance with OECD TG 471; positive and negative controls used	Not mutagenic, with or without metabolic activation, in all tester strains; controls yielded expected results	[2]
Charcoal (batch with C-fix – 88.7%)	50 - 5000 µg/plate with plate incorporation method; 313 - 5000 µg/plate with pre-incubation method	ethanol	*S. typhimurium* TA97a, TA98, TA100, TA102, and TA1335	Bacterial reverse mutation assay, with and without S9 metabolic activation; in accordance with OECD TG 471; positive and negative controls used	Not mutagenic, with or without metabolic activation, in all tester strains; controls yielded expected results	[2]
Charcoal (batch with C-fix = 83.26%)	50 - 5000 µg/plate with plate incorporation method	dimethyl sulfoxide (DMSO)	*S. typhimurium* TA98, TA100, TA1535, and TA153 and *Escherichia coli* WP2 uvrA	Bacterial reverse mutation assay, with and without S9 metabolic activation; in accordance with OECD TG 471; positive and negative controls used	Not mutagenic, with or without metabolic activation, in all tester strains; controls yielded expected results	[2]
Charcoal (total carbon 83.11%, C-fix = 75.72%)	50 - 5000 µg/plate with plate incorporation method and pre-incubation method	DMSO	*S. typhimurium* TA97a, TA98, TA100, TA102, and TA1335	Bacterial reverse mutation assay, with and without S9 metabolic activation; in accordance with OECD TG 471; positive and negative controls used	Not mutagenic, with or without metabolic activation, in all tester strains; controls yielded expected results	[2]
Charcoal (batch with C-fix = 80.5%)	1250, 2500, or 5000 µg/ml	Dulbecco's Modified Eagle medium	V79 male Chinese hamster lung cells	Mammalian chromosome aberration test in accordance with OECD TG 473, with and without S9 metabolic activation; positive and negative controls used	Not clastogenic; test material did not induce structural chromosome aberrations, with or without metabolic activation; controls yielded expected results	[2]

Table 4. Genotoxicity studies.

Test Article	Concentration/Dose	Vehicle	Test System	Procedure	Results	Reference
Charcoal (batch with C-fix = 83.3%)	3-h exposure with and without S9: 150, 500, 1500, or 5000 µg/ml mg/ml 24-h exposure without S9: 500, 1000, 2500, or 5000 µg/ml	Dulbecco's Modified Eagle medium	V79 male Chinese hamster lung cells	Mammalian chromosome aberration test in accordance with OECD TG 473, with and without S9 metabolic activation; positive and negative controls used	Not clastogenic; test material did not induce structural chromosome aberrations, with or without metabolic activation; controls yielded expected results	[2]
Charcoal (total carbon 83.11%, C-fix = 75.75%)	3-h exposure with and without S9 100, 300, or 1000 µg/ml 24-h exposure without S9 100, 300, or 1000 µg/ml	DMSO	human peripheral blood lymphocytes	Mammalian chromosome aberration test in accordance with OECD TG 473, with and without S9 metabolic activation; positive and negative controls used	Not mutagenic; test material did not induce any biologically significant or concentration-related increase in the incidence of chromosome aberrations, with or without metabolic activation; controls yielded expected results	[2]
Charcoal (batch with C-fix = 80.5%)	128, 320, 800, 2000 µg/ml	acetone/n-hexane 50:50 (v:v)	mouse lymphoma L5178Y $TK^{+/-}$ cells	Mammalian cell gene mutation assay in accordance with OECD TG 476; with and without S9 metabolic activation; positive and negative controls used	Not mutagenic; test material did not induce gene mutations, with or without metabolic activation; controls yielded expected results	[2]
Charcoal (no further details)	up to 2400 µg/ml	not reported	mouse lymphoma L5178Y TK+/- cells	Mammalian cell gene mutation assay in accordance with OECD TG 476; with and without S9 metabolic activation; positive and negative controls used	Not mutagenic; test material did not induce gene mutations, with or without metabolic activation; controls yielded expected results	[2]
Charcoal (batch with C-fix = 83.3%)	125 - 2000 µg/ml	DMSO	human peripheral blood lymphocytes	Mammalian cell micronucleus test in accordance with OECD TG 487; with and without metabolic activation; positive and negative controls used	Not genotoxic, with or without metabolic activation; controls yielded expected results	[2]
Charcoal Powder (bamboo sourced)	8-5000 µg/plate with plate incorporation method	ultrapure water	*S. typhimurium* TA97, TA98, TA100, and TA102	Bacterial reverse mutation assay, with and without S9 metabolic activation; in accordance with OECD TG 471; positive and negative controls used	Not mutagenic, with or without metabolic activation, in all tester strains; controls yielded expected results	[19]
IN VIVO						
Charcoal Powder (bamboo-sourced)	0, 2810, 5620, or 11,240 mg/kg bw/d	ultrapure water	Groups of 5 male and 5 female Kunming mice	Comet assay in accordance with OECD draft guideline for the Testing of Chemicals – In Vivo Mammalian Alkaline Comet Assay; animals received test material for 4 d at 24-h intervals via gavage (2 ml/kg); clinical signs of toxicity and mortality were assessed; mice were killed 3 h after last dose; positive and negative controls used; liver cells analyzed in assay	Not mutagenic; no statistically significant differences in % tail DNA, tail length, and Olive tail moment indices between the negative control and the groups treated with the test material; no clinical signs of toxicity, including the positive control; positive control yielded expected results in assay	[19]
Charcoal Powder (bamboo-sourced)	0, 2810, 5620, or 11,240 mg/kg bw/d	ultrapure water	Groups of 5 male and 5 female Kunming mice	Mammalian erythrocyte micronucleus test in accordance with OECD TG 474; animals received test material for 4 d at 24-h intervals via gavage (2 ml/kg); clinical signs of toxicity and mortality were assessed; mice were killed 3 h after last dose; positive and negative controls used; bone marrow cells analyzed; 2000 polychromatic erythrocytes per animal evaluated for the presence of micronuclei and the ratio of polychromatic erythrocytes in 1000 normochromatic erythrocytes per animal were evaluated	Not mutagenic; no increase of micronuclei in the groups treated with the test material, comparable to negative control; no clinical signs of toxicity, including the positive control; positive control yielded expected results	[19]

Table 5. Dermal irritation and sensitization studies.

Test Article	Vehicle	Concentration/Dose	Test Population	Procedure	Results	Reference
IRRITATION						
IN VITRO						
Charcoal (batch with C-fix = 73.3%)	none	100%	Reconstructed human epidermis	Reconstructed human epidermis model test; positive and negative controls used	Not irritating; controls yielded expected results	[2]
Charcoal (batch with C-fix = 80.5%)	none	100%	Reconstructed human epidermis	Reconstructed human epidermis model test; positive and negative controls used	Not irritating; controls yielded expected results	[2]
Charcoal (batch with C-fix = 88.7%)	none	100%	Reconstructed human epidermis	Reconstructed human epidermis model test; positive and negative controls used	Not irritating; controls yielded expected results	[2]
ANIMAL						
Charcoal (bath with C-fix = 80.5%)	none	100%	3 male New Zealand White rabbits	Primary skin irritation test in accordance with OECD TG 404; single dose of 0.5 g applied moistened to test site and occluded; test material removed by rinsing with water after 4 h; signs of irritation were assessed at 1, 24, 48, and 72 h post-patch removal; untreated skin was negative control	Not irritating; no signs of erythema or edema observed	[2]
SENSITIZATION						
ANIMAL						
Charcoal (batch with C-fix = 73.3%)	propylene glycol	0, 2.5, 5, or 10% w/w	Groups of 4 female CBA/CaOlaHsd mice	LLNA in accordance with OECD TG 429; positive and negative controls used	Not sensitizing; stimulation indices (SI) for 2.5, 5, and 10% test material were 0.65, 0.72, and 1.11, respectively; an effective concentration inducing a stimulation index of 3 (EC_3) could not be calculated; controls yielded expected results	[2]
Charcoal (batch with C-fix = 80.5%)	propylene glycol	0, 2.5, 5, or 10% w/w	Groups of 4 female CBA/CaOlaHsd mice	LLNA in accordance with OECD TG 429; positive and negative controls used	Not sensitizing; SI for 2.5, 5, and 10% test material were 1.04, 0.87, and 1.30, respectively; an EC_3 could not be calculated; controls yielded expected results	[2]
Charcoal (batch with C-fix = 88.7%)	propylene glycol	0, 2.5, 5, or 10% w/w	Groups of 4 female CBA/CaOlaHsd mice	LLNA in accordance with OECD TG 429; positive and negative controls used	Not sensitizing; SI for 2.5, 5, and 10% test material were 1.25, 1.38, and 1.40, respectively; an EC_3 could not be calculated; controls yielded expected results	[2]

Table 6. Ocular irritation studies.

Ingredient	Concentration/Dose	Vehicle	Test Population	Procedure	Results	Reference
			IN VITRO			
Charcoal (batch with C-fix = 73.3%)	100%	None	6 Lohmann Selected Leghorn chicken eggs	HET-CAM method; membrane exposed to single application of ~50 mg for 5 min; negative and positive controls used	Not irritating; controls yielded expected results	[2]
Charcoal (batch with C-fix = 80.5%)	100%	None	6 Lohmann Selected Leghorn chicken eggs	HET-CAM method; membrane exposed to single application of ~50 mg for 5 min; negative and positive controls used	Not irritating; controls yielded expected results	[2]
Charcoal (batch with C-fix = 88.7%)	100%	None	6 Lohmann Selected Leghorn chicken eggs	HET-CAM method; membrane exposed to single application of ~50 mg for 5 min; negative and positive controls used	Not irritating; controls yielded expected results	[2]
			ANIMAL			
Charcoal (batch with C-fix = 80.5%)	100%	None	3 male New Zealand White rabbits	Ocular irritation study in accordance with OECD TG 405; observations made 1, 24, 48, and 72 h and 7 d after instillation	Not irritating according to EU criteria; slight to severe conjunctival irritant effects fully reversible within 1 wk, no irritant reaction observed in cornea and iris	[2]

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