Safety Assessment of Boron Nitride as Used in Cosmetics

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date to comment on this safety assessment and to identify additional published data that should be included or provide unpublished data which can be made public and included.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 All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a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

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INTRODUCTION

This Scientific Literature Review is the first step in reviewing the safety of boron nitride as used in cosmetics. Boron nitride is an inorganic compound reported to function in cosmetics as a slip modifier.[1] Based on that function, it appears that hexagonal boron nitride is the compound used in cosmetics. However, in the absence of data on hexagonal boron nitride, this review includes safety data on cubic boron nitride as well as boron nitride nanotubes. At this time, the Cosmetic Ingredient Review (CIR) is unsure if data on boron nitride in these forms are applicable to the safety of the cosmetic use of boron nitride, but it is being presented in the absence of other applicable data. Comments on what form(s) of boron nitride is used in cosmetics are welcomed.

CHEMISTRY

Definition and Structure

Boron nitride (CAS No. 10043-11-5) is an inorganic compound[1] with a flat, hexagonal crystal similar to graphite, but with the carbon atoms replaced by boron and nitrogen atoms.[2,3] The alternate boron and nitrogen atoms are linked to form inter-locking hexagonal rings with three boron atoms and three nitrogen atoms, and the layers are held together by van der Waals forces.[4] (Figure 1). There is no boron-nitrogen bonding between the layers.[5] The bond length is 1.466 Å and the interlayer spacing is 3.331 Å.[6] A spherical form (with a hexagonal crystal structure) is also available.[7]

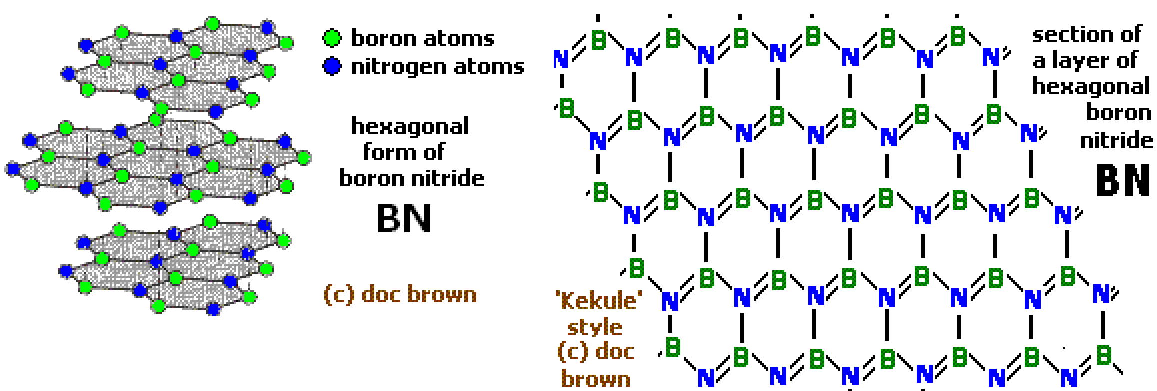

Figure 1. Hexagonal boron nitride.[4]

Boron nitride can also be in cubic form in which alternately linked boron and nitrogen atoms form a tetrahedral bond network, similar to carbon atoms in diamond.[4] (Figure 2).

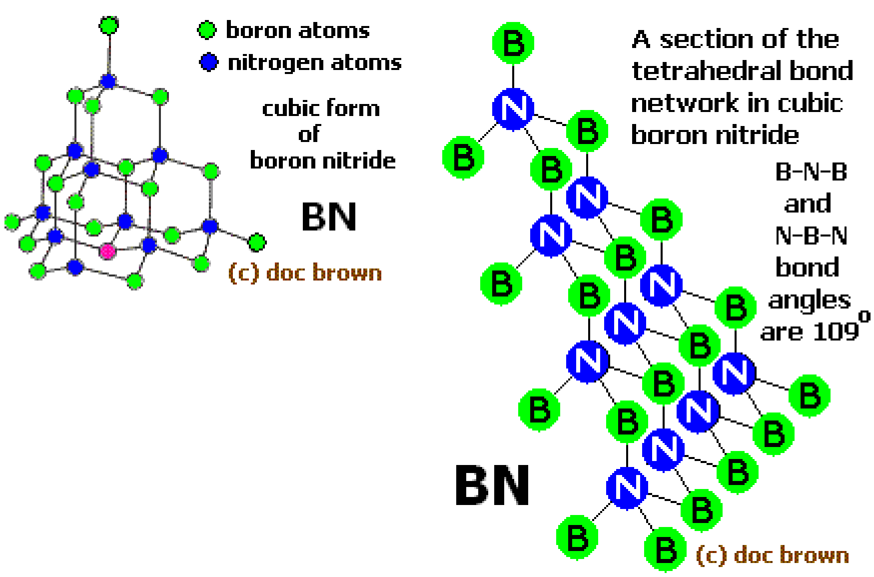

Figure 2. Cubic boron nitride.[4]

Physical and Chemical Properties

The available physical and chemical properties data are provided in Table 1. Hexagonal boron nitride has a plate-like microstructure and layered lattice structure similar to graphite.[8] Cubic boron nitride is the second hardest material known (with diamond being the hardest).[4] The mean particle size of cosmetic-grade hexagonal boron nitride powder varies by trade names and grade, with sizes of 1-47 µm reported.[3,5,9-14]

Method of Manufacture

Cosmetic-grade hexagonal boron nitride is produced by a synthesis of borax and a nitrogen source at a high temperature, resulting in a lamellar structure.[5] Another source reports that hexagonal boron nitride powder is synthesized by nitridation or ammonalysis of boric oxide at elevated temperature.[8]

Boron nitride nanotubes, as multi-walled tubes with inner diameters of 1-3 nm and lengths up to 200 nm, were produced in a carbon-free plasma-discharge between a BN-packed tungsten rod and a cooled copper electrode.[15]

Composition/Impurities

The typical chemical analysis of hexagonal cosmetic-grade boron nitride is: ≥98-99.8% BN, 0.2-1.6% O_2, 0.02-0.1% B_2O_3, and <1 ppm metals (as Hg, As. Pb).[3,5,9-12]

USE

Cosmetic

Boron nitride is reported to function in cosmetics as a slip modifier.[1] The Food and Drug Administration (FDA) collects information from manufacturers on the use of individual ingredients in cosmetics as a function of cosmetic product category in its Voluntary Cosmetic Registration Program (VCRP). VCRP data obtained from the FDA in 2012 report that boron nitride is used in 483 cosmetic formulations[16] and data received in response to a survey of the maximum reported use concentration by category conducted by the Personal Care Products Council (Council) report that it is used at concentrations up to 25%.[17] The highest concentration of use is in eye shadow formulations.

Products containing boron nitride are reported to be used on baby skin (in a lotion, oil, powder, or cream), may be applied to the eye area or mucous membranes, could possible ingested, or may possibly be inhaled. Boron nitride is reported to be used at up to 25% in eye product formulations, at 2% in lipstick formulations, up to 16% in powders, and at up to 0.9% in fragrance preparations. Although use in baby products was reported to the VCRP, no concentration of use data were reported by industry. In practice, 95% to 99% of the particles released from cosmetic sprays have aerodynamic equivalent diameters in the 10 to 110 µm range.[18,19] Therefore, most particles incidentally inhaled from these sprays are deposited in the nasopharyngeal region and are not respirable.[20,21]

Boron nitride is listed in the European Union inventory of cosmetic ingredients; no restrictions are specified.[22]

Non-Cosmetic Use

Hexagonal boron nitride can be used as an electrical insulator; as thermocouple protection sheaths, crucibles and linings for reaction vessels; and as a coating for refractory molds used in glass forming and in superplastic forming of titanium.[8] It can also be incorporated in ceramics, alloys, resins, plastics, and rubber to give them self-lubricating properties.[4] Hexagonal boron nitride is used the formulation of coatings and paints for high temperature applications.[23] It is also used as a substrate for semi-conductors, lens coatings, and transparent windows.

Hexagonal boron nitride can be made in single layers to form nanotubes,[4] and bundles of boron nanotubes are used for wire sleeving. Boron nitride nanotubes are being produced commercially.[24]

Cubic boron nitride is used as an abrasive and wear-resistant coating; it is used for cutting tools and abrasive components for shaping/polishing with low carbon ferrous metals.[4]

TOXICOKINETICS

Published toxicokinetics studies were not found.

TOXICOLOGICAL STUDIES

Single Dose (Acute) Toxicity

Parenteral

Intravenous (i.v.) injection of boron nitride nanotubes did not produce toxicity in rabbits.[25] Three New Zealand White rabbits received a single 1 mg/kg i.v. dose of glycol chitosan-coated (G-chitosan) boron nitride nanotubes in physiological saline at a concentration of 1 mg/ml. Two control rabbits were given an i.v. dose of G-chitosan only. Blood samples were collected at 0, 2, 24, and 72 h. No signs of toxicity were observed, and with the exception of an increased platelet count at 72 h (that was still in the reference range), no differences in hematological parameters were observed between treated and control animals.

Repeated Dose Toxicity

Published repeated dose toxicity studies were not found.

Ocular Irritation

Published ocular irritation studies were not found.

Cytotoxicity

Contradictory results have been reported on the cytotoxicity of boron nitride nanotubes. In this study, boron nitride nanotubes were found to be cytotoxic when evaluated using lung epithelial cells (A549), alveolar macrophages (RAW 264.7), and fibroblast cells (3T3-L1), as well as in human embryonic kidney cells (HEK 293).[24] Tween 80 was used as the dispersing agent and yielded a suspension of individual nanotubes with long-term stability; the typical diameters were less than 80 nm (average of ~50 nm) and the average length was ~10 µm. Cells were exposed to 0.02, 0.2, and 20 µg/ml of the nanomaterial. In an MTT (3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyl tetrazolium bromide) assay, 2 µg/ml boron nitride nanotubes produced a decrease of the MTT signal when compared to untreated cells. At 48-h, this result was time-, dose-, and cell type-dependent, with the greatest effect observed in cells with high endocytic (phagocytic) activity, i.e. macrophages, and the lowest toxicity observed in cells with the lowest endocytic activity, i.e., HEK 293 cells. A fluorometric DNA assay and fluorometric microculture assay were performed with lung A549 epithelial cells and RAW 264.7 macrophage cells to confirm these results. Similar results were obtained; a decrease of 60-80% in cell number was observed with 2 µg/ml macrophage cells and a 30% loss was observed with 20 µg/ml A549 epithelial cells.

The results presented above contradict earlier studies on boron nitride nanotubes that did not report cytotoxicity. In one study using human neuroblastoma SH-SY5Y cells, up to 100 µg/ml G-chitosan-coated boron nanotubes were tested in two cell proliferation assays, an MTT-assay and a WST-1 (2-(4-iodophenyl)-3-(4-nitrophneyl)-5-(2,4-disulfophenyl-2*H*-tetrazoilium monosodium salt) assay, in a DNA content assessment, a viability/cytotoxicity assay, an early apoptosis detect assay, and a reactive oxygen species (ROS) assay.[26] A statistically significant reduction in MTT was observed at concentration of 20 µg/ml boron nitride nanotubes, but this reduction was not observed with G-chitosan alone or in WST-1. The researchers stated that, most likely, the boron nitride nanotubes interact with some tetrazolium salts, such as MTT, but not with others, such as WST-1, suggesting that the interference is due to the water-insoluble nature of MTT-formazan. The boron nitride nanotubes did not affect the DNA concentration, cell viability, apoptosis, or ROS formation.

In another study, HEK 293 cells were cultured with 100 mg/ml boron nitride tubules, which formed aggregates in culture media.[27] Cells cultured with boron nitride nanotubules were not different from cells cultured in media. Similar results were found with Chinese hamster ovary (CHO) cells.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Published reproductive and developmental toxicity studies were not found.

GENOTOXICITY

Published genotoxicity studies were not found.

CARCINOGENICITY

Published carcinogenicity studies were not found.

IRRITATION AND SENSITIZATION

Published dermal irritation and sensitization studies were not found.

INFORMATION SOUGHT

The CIR is seeking clarification as to what form/forms of boron nitride is/are used in cosmetics. Additionally, at a minimum, the following information on boron nitride in the form that is used in cosmetics is being sought for use in the resulting safety assessment:

1. toxicokinetics data;
2. repeated-dose toxicity data;
3. inhalation toxicity data;
4. reproductive/developmental toxicity data;*
5. genotoxicity data; if positive, carcinogenicity data may be needed;
6. irritation and sensitization data on cosmetic-grade boron nitride; and,
7. as boron nitride is used in eye shadows at up to 25%, ocular irritation data, if available.

*While these data may not be crucial if these ingredients have no appreciable dermal penetration, if available, they would improve the resulting safety assessment.

SUMMARY

Boron nitride is an inorganic compound that can be hexagonal or cubic in form. Hexagonal boron nitride is similar to graphite, while cubic boron nitride is similar to diamond. The mean particle size of cosmetic-grade hexagonal boron nitride powder varies by trade name and grade, with mean particle sizes of 1-47 µm reported.

Boron nitride is reported to function as a slip modifier in cosmetic. VCRP data report 483 uses of boron nitride, and concentrations of use of up to 25% were reported by the cosmetics industry, with the highest use concentration reported in eye shadow formulations.

A single intravenous injection of 1 mg/kg G-chitosan-coated boron nitride nanotubes did not produce toxicity in rabbits.

Contradictory results have been reported on the cytotoxicity of boron nitride nanotubes. One study found that boron nitride nanotubes were cytotoxic when evaluated using lung epithelial A549 cells, alveolar macrophages RAW 264.7 cells, fibroblast 3T3-L1 cells, and human embryonic kidney HEK 293 cells, while another study reported that boron nitride was not cytotoxic to HEK 293 or CHO cells. In human neuroblastoma SH-SY5Y cells, up to 100 µg/ml G-chitosan-coated boron nanotubes caused a statistically significant reduction in MTT at a concentration of 20 µg/ml boron nitride nanotubes, but this reduction was not observed with G-chitosan alone or in WST-1 and was attributed the water-insoluble nature of MTT-formazan. Boron nitride nanotubes did not affect DNA concentration, cell viability, apoptosis, or ROS formation in these cells.

TABLES

Table 1. Chemical and physical properties

Property	Description	Reference
appearance	white powder; hexagonal or cubic crystals white, photostable, odorless powder (hexagonal, cosmetic grade) white, photostable, granular powder with a soft, flowable texture (spherical morphology)	28 29 7
molecular weight	24.818	28
melting point	2967 °C	28
mean particle size	1-47 µm (varies by trade name and grade) 30 µm (spherical morphology)	3,5,9-14 7
density	2.18 g/cm^3 2.26 g/cm^3 (hexagonal, cosmetic-grade)	28 5
surface area	0.82-30 m^2/g (hexagonal; varies by grade) 4 m^2/g (spherical morphology)	3,5,9-12 7
refractive index	1..74	5
solubility	insoluble in water and in acid solutions	28
stability	chemically inert and stable	5
coefficient of friction	<0.3	5

Table 2. Frequency and concentration of use according to duration and type of exposure

	# of Use[16]	*Max. Conc. of Use (%)*[17]
Totals*	**483**	**0.01-25**
Duration of Use		
Leave-On	*481*	*0.01-25*
Rinse Off	*2*	*0.05*
Diluted for (Bath) Use	*NR*	*NR*
Exposure Type		
Eye Area	180	0.08-25
Incidental Ingestion	4	2
Incidental Inhalation - Spray	12[a]	0.8-0.9
Incidental Inhalation - Powder	90	1-16
Dermal Contact	473	0.01-25
Deodorant (underarm)	NR	NR
Hair - Non-Coloring	4	0.05
Hair-Coloring	NR	NR
Nail	2	2
Mucous Membrane	4	2
Baby Products	1	NR

* 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.
[a] Includes fragrance and suntan products
NR – none reported

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