
Safety Assessment of Boron Nitride as Used in Cosmetics

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ABSTRACT

The CIR Expert Panel assessed the safety of boron nitride as used in cosmetics, concluding that this ingredient is safe in the present practices of use and concentration in cosmetic formulations. Boron nitride, an inorganic compound with a crystalline form that can be hexagonal or cubic, is reported to function in cosmetics as a slip modifier (i.e., it has a lubricating effect). The highest reported concentration of use of boron nitride is 25% in eye shadow formulations. The International Cosmetic Ingredient Dictionary and Handbook does not specify which crystal form(s) is (are) used in cosmetics, but it is presumed that the hexagonal form is used in cosmetics. Although boron nitride nanotubes are produced, boron nitride is not listed as a nanomaterial used in cosmetic formulations. The Panel reviewed available chemistry, animal data, and clinical data in making its determination of safety.

INTRODUCTION

This report reviews the safety of boron nitride as used in cosmetics. Boron nitride is an inorganic compound reported to function in cosmetics as a slip modifier. Although the *International Cosmetic Ingredient Dictionary and Handbook* does not specify which crystal form(s) is (are) used in cosmetics, it is presumed that hexagonal boron nitride is used. In the *2011 Associations Survey of Nanomaterials Used in Cosmetic Products*, a report prepared for the International Cooperation on Cosmetic Regulation by a working group of the Personal Care Products Council (Council), Canadian Cosmetic Toiletry, and Fragrance Association, COLIPA (now known as Cosmetics Europe), and the Japanese Cosmetic Industry Association, boron nitride is not listed as a nanomaterial used in cosmetic formulations.¹ This safety assessment prepared by the Cosmetic Ingredient Review (CIR) includes (limited) toxicity data on boron nitride nanotubes, because even though boron nitride is not thought to be a nanomaterial used in cosmetic formulations, these data demonstrate the lack of toxicity of boron nitride.

CHEMISTRY

Definition and Structure

Boron nitride (CAS No. 10043-11-5) is an inorganic compound, with the chemical formula BN.² The compound can assume three crystal polymorphs. One is a flat, hexagonal crystalline structure, similar to graphite, except that the carbon atoms are replaced by boron and nitrogen atoms.^{3,4} The alternate boron and nitrogen atoms form interlocking hexagonal rings, each with three boron atoms and three nitrogen atoms, and the layers are held together by van der Waals forces (Figure 1).⁵ There is no boron-nitrogen bonding between the layers.⁶ A spherical form, with a hexagonal crystal structure, also can occur.⁷ Additionally, boron nitride can be in cubic form in which alternately-linked boron and nitrogen atoms form a tetrahedral bond network (Figure 2).⁵

Physical and Chemical Properties

The available physical and chemical properties of boron nitride are provided in Table 1. The three-ring, layered structure gives hexagonal boron nitride a lubricating effect, high thermal stability, and oxidation resistance.⁸ The mean particle size of cosmetic-grade hexagonal boron nitride powder varies by trade names and grade, with sizes of 1-47 μm reported.^{4,6,9-14}

Cubic boron nitride is the second hardest material known, with diamond being the hardest.⁵

Method of Manufacture

Cosmetic-grade hexagonal boron nitride is synthesized using borax and a nitrogen source at a high temperature, resulting in a lamellar structure.⁶ Industrial synthesis of hexagonal boron nitride powder is based on a two-stage process.⁸ First, at approximately 900°C, a boron source such as boron oxide or boric acid is converted in a reaction with a nitrogen source, mostly melamine or urea or, possibly, ammoniac, to amorphous boron nitride. In the second step, crystallization occurs at temperatures usually >1600°C in a nitrogen atmosphere; a transition into hexagonal boron nitride occurs. At high temperatures (600 - 2000 °C) and pressures (50 – 200 kbar), hexagonal boron nitride can be converted to the cubic phase.¹⁵

Composition/Impurities

The typical chemical analysis of hexagonal cosmetic-grade boron nitride is: $\geq 98-99.8\%$ BN, 0.2-1.6% O₂, 0.02-0.1% B₂O₃, and <1 ppm metals (as Hg, As, Pb).^{4,6,9-12}

USE

Cosmetic

Boron nitride is reported to function in cosmetics as a slip modifier, which means it purportedly helps other substances to flow more easily and more smoothly, without reacting chemically, much like graphite.^{2,16} This ingredient is a type of ceramic, having the smoothness and the chemical and thermal inertness associated with most ceramics.⁹ 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 2013 reported that boron nitride is used in 643 cosmetic formulations.¹⁷ Data received in response to a survey of the maxi-

imum reported use concentration by category conducted by the Personal Care Products Council (Council) reported that boron nitride is used at concentrations up to 25%; the highest concentration of use is in eye shadow formulations.¹⁸

Although use in baby products was reported to the VCRP, concentration-of-use data were not reported by industry. Products containing boron nitride may be applied to the eye area ($\leq 25\%$ in eye product formulations), could possibly be ingested (2% in lipstick formulations), or may possibly be inhaled ($\leq 16\%$ in powders and at up to 0.9% in fragrance preparations). In practice, 95% to 99% of the particles released from cosmetic sprays have aerodynamic equivalent diameters in the 10 to 110 μm range.^{19,20} Therefore, most particles incidentally inhaled from these sprays are deposited in the nasopharyngeal region and are not respirable to any appreciable amount.^{21,22}

Boron nitride is listed in the European Union inventory of cosmetic ingredients; no restrictions are specified.²³

Non-Cosmetic Use

The properties of hexagonal boron nitride allow for its use in a number of technological processes. Different forms of hexagonal boron nitride are used for different applications: boron nitride, compacted by hot pressing or hot isostatic pressing, can be used in making shaped components for various industries; boron nitride coating systems using suspensions and sprays are used to selectively change the properties of substrate surfaces; and powdered boron nitride coating systems using powders and granules can be used in thermal management.⁸ Hexagonal boron nitride can be used as an electrical insulator; as thermocouple protection sheaths, in crucibles and linings for reaction vessels; and as a coating for refractory molds used in glass forming and in superplastic forming of titanium.²⁴ It can also be incorporated in ceramics, alloys, resins, plastics, and rubber to give them self-lubricating properties.⁵ Hexagonal boron nitride is used in the formulation of coatings and paints for high temperature applications, and it is also used as a substrate for semi-conductors, lens coatings, and transparent windows.²⁵

Hexagonal boron nitride can be made in single layers to form nanotubes, and bundles of boron nanotubes are used for wire sleeving.⁵ Boron nitride nanotubes are being produced commercially.²⁶

Cubic boron nitride is used as an abrasive and wear-resistant coating; it is used for cutting tools and as abrasive components for shaping/polishing with low carbon ferrous metals.⁵

TOXICOKINETICS

In a pharmacokinetics study, four New Zealand white rabbits were given an intravenous (i.v.) injection of 10 mg/kg bw sterilized glycol chitosan-coated (G-chitosan) boron nitride nanotubes in physiological solution.²⁷ Blood samples were taken at various intervals for up to 10 h. Boron concentration was measured as an indicator of boron nitride nanotube presence. The terminal half-life was 98 ± 37 min. The researcher stated that an absence of multi-exponential kinetic components indicated no significant temporary accumulation of boron nitride nanotubes in tissues. The researchers also stated that the data suggested a “relatively high” clearance of boron nitride nanotubes from the blood and a quick distribution and/or excretion, but also noted that the functionalization of the nanoparticles has a role in their behavior at a systemic level.

TOXICOLOGICAL STUDIES

Single Dose (Acute) Toxicity

Parenteral

A single i.v. injection of 1, 5, or 10 mg/kg bw coated boron nitride nanotubes did not produce toxicity in rabbits.^{27,28} In a pilot study, three New Zealand White rabbits received a single 1 mg/kg i.v. dose of G-chitosan boron nitride nanotubes in physiological saline at a concentration of 1 mg/ml.²⁸ 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.

In a follow-up study, groups of three male New Zealand white rabbits were given a single i.v. dose of 5 or 10 mg/kg sterilized G-chitosan boron nitride nanotubes in physiological solution (average hydrodynamic size 500 nm).²⁷ The test volume was 10 mg/ml. Blood samples were collected 0, 1, 3, and 7 days after dosing. No signs of toxicity were observed, and results of the hematological analysis were within normal limits.

Repeated Dose Toxicity

Parenteral

G-chitosan boron nitride nanotubes also did not produce toxicity in a repeated dose study.²⁷ Three male New Zealand white rabbits were dosed by i.v. injection with 5 mg/kg bw/day sterilized G-chitosan boron nitride nanotubes in physiological solution for three consecutive days, and blood samples were taken as above. As in the single-dose studies, no signs of toxicity were observed and results of the hematological analysis were within normal limits.

Cytotoxicity

Contradictory results have been reported on the cytotoxicity of boron nitride nanotubes. In one study, boron nitride nanotubes (not coated) 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).²⁶ 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, 2, and 20 $\mu\text{g/ml}$ of the nanomaterial. In an MTT (3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyltetrazolium bromide) assay of cell proliferation, 2 $\mu\text{g/ml}$ 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; exposures of 0.2, 2, and 20 $\mu\text{g/ml}$ nanomaterial were used. Similar results were obtained; a decrease of 60-80% in viable cell number was observed with 2 $\mu\text{g/ml}$ in macrophage cells and a 30% loss was observed with 20 $\mu\text{g/ml}$ in 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 $\mu\text{g/ml}$ G-chitosan-coated boron nanotubes were tested in two cell proliferation assays, an MTT-assay and a WST-1 (2-(4-iodophenyl)-3-(4-nitrophenyl)-5-(2,4-disulfophenyl)-2H-tetrazolium monosodium salt) assay, in a DNA content assessment, a viability/cytotoxicity assay, an early apoptosis detect assay, and a reactive oxygen species (ROS) assay.²⁹ A statistically significant reduction in MTT was observed at a concentration of 20 $\mu\text{g/ml}$ 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.³⁰ Cells cultured with boron nitride nanotubules were not different from cells cultured in media. Similar results were found with Chinese hamster ovary (CHO) cells.

The Expert Panel noted that all of these studies should be viewed with caution because the very low solubility of the test compounds requires solution vehicles that could bias the results. The exposures to cells *in vitro* are very different from the ways in which boron nitride might be presented to skin or epithelia in humans.

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

Dermal

Human

Boron nitride was a weak skin irritant in a 24-h human patch test.³¹ Occlusive patches of boron nitride, 50% in olive oil, were applied to 20 subjects. Two subjects exhibited a \pm response. (Additional details were not provided).

Eye shadow formulations containing 13% boron nitride, tested at a concentration of 70% in squalane oil,³² and 18.7% boron nitride, tested neat,³³ and face powder formulations containing 16% boron nitride,^{34,35} were not dermal irritants or sensitizers in human repeated insult patch tests (HRIPTs). The details of these studies are presented in Table 3.

Ocular

Non-Human

A short-term exposure (STE) test was performed to evaluate the irritation potential of boron nitride; an STE is an *in vitro* assay for ocular irritation that assesses cytotoxicity in a rabbit corneal cell line (SIRC cells) following a 5-min treatment.³⁶ Boron nitride, tested at 0.05 and 5% in mineral oil, was ranked a minimal irritant in an STE test.³¹

Results of chorioallantoic membrane (CAM) assays also predicted that boron nitride is not an ocular irritant.³¹ Boron nitride was assayed at 50% in Vaseline using the HET-CAM method (i.e., hen's egg test-CAM, which determines hemorrhage, lysis,

and coagulation in the CAM of the egg after exposure to test chemicals³⁷) and the CAM-TB method (i.e., CAM-trypan blue staining, which measures the amount of trypan blue adsorbed onto the CAM as the endpoint of the assay³⁷).

Human

An eye shadow containing 13% boron nitride did not cause any adverse effects in a 2-wk use study.³⁸ Thirty female subjects completed the study, 17 of whom wore contact lenses. The eye shadow was applied at least one time daily.

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 nanotubes are produced commercially; however, boron nitride is not listed as a nanomaterial used in cosmetic formulations.

Boron nitride is reported to function as a slip modifier in cosmetics. VCRP data report 643 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.

In a pharmacokinetic study in which four New Zealand white rabbits were given an i.v. injection of 10 mg/kg bw sterilized glycol chitosan-coated (G-chitosan) boron nitride nanotubes in physiological solution, no significant temporary accumulation of boron nitride nanotubes in tissues was found. The researchers concluded there was a relatively high clearance of boron nitride nanotubes from the blood and a quick distribution and/or excretion.

A single i.v. injection of 1, 5, or 10 mg/kg G-chitosan boron nitride nanotubes did not produce toxicity in rabbits. Toxicity also was not observed following repeated dosing with 5 mg/kg bw/day sterilized G-chitosan boron nitride nanotubes in physiological solution for 3 consecutive days.

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 $\mu\text{g/ml}$ G-chitosan-coated boron nanotubes caused a statistically significant reduction in MTT at a concentration of 20 $\mu\text{g/ml}$ 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.

Boron nitride, 50% in olive oil, was a weak skin irritant in a 24-h human patch test. Eye shadow formulations containing 13% boron nitride, tested at a concentration of 70% in squalane oil, and 18.7% boron nitride, tested neat, and face powder formulations containing 16% boron nitride, were not dermal irritants or sensitizers in human repeated insult patch tests.

In non-human testing, boron nitride, tested at 0.05 and 5% in mineral oil, was ranked a minimal irritant in an STE test. Additionally, boron nitride, assayed at a concentration of 50% in Vaseline, was negative in a HET-CAM assay and a CAM-TB assay. In human testing, an eye shadow containing 13% boron nitride did not produce any adverse effects in a 2-wk use study.

DISCUSSION

Boron nitride is an inorganic compound that can assume different crystal polymorphs which are insoluble and stable and not likely to penetrate the stratum corneum.

Human repeat insult patch test data were available on formulations that contained boron nitride at concentrations up to 18.7%. Although sensitization data were not provided at the maximum reported leave-on use concentration of 25%, the Expert Panel concluded that the existing data were adequate. At a 50% concentration, boron nitride caused minimal irritation. At 18.7%, it was not a sensitizer, nor would it be expected to sensitize given its inability to penetrate the stratum corneum. Additionally, boron nitride is not expected to be an ocular irritant at the maximum reported concentration of use; in a 2-wk use study, an eye shadow containing 13% boron nitride did not cause any adverse effects.

The Expert Panel also stated that although there are data gaps, this ingredient is chemically inert and completely insoluble, and the extended hexagonal crystal lattice structure makes boron nitride a very large molecule that is not expected to penetrate the stratum corneum. Even if it were to penetrate, it would not be expected to have chemical activity in biological systems. Although boron nitride is not reported to be used in nanomaterial form in cosmetic formulations, the lack of toxicity observed in single- and repeated-dose intravenous studies with coated boron nitride nanotubes further supports the safety of boron nitride in other forms. Also, the fact that boron nitride is not expected to penetrate the skin precludes the need for repeated dose toxicity, reproductive and developmental toxicity, and carcinogenicity studies.

The Panel discussed the issue of incidental inhalation exposure to boron nitride from powders and from products that may be aerosolized. Boron nitride is reportedly used at up to 16% in products that may become airborne (i.e., in face powders), but

only at very low concentrations in cosmetic products that may be aerosolized (i.e., up to 0.9% in fragrance preparations). Because boron nitride is not expected to have chemical activity in biological systems, particles deposited in the nasopharyngeal or bronchial regions of the respiratory tract present no toxicological concerns. Coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products that may be aerosolized is available at <http://www.cir-safety.org/cir-findings>.

CONCLUSION

The CIR Expert Panel concluded that boron nitride is safe in cosmetics in the present practices of use and concentration described in this safety assessment.

FIGURES

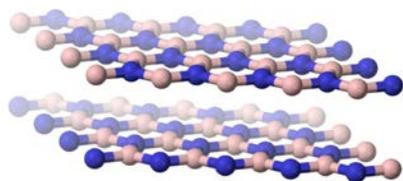


Figure 1. Hexagonal boron nitride.¹⁵

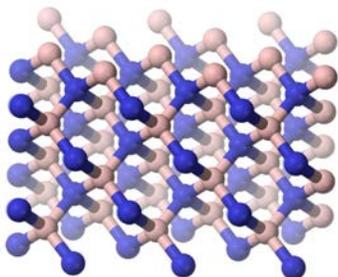


Figure 2. Cubic boron nitride.¹⁵

TABLES

Table 1. Chemical and physical properties

Property	Description	Reference
appearance	white powder; hexagonal or cubic crystals	39
	white, photostable, odorless powder (hexagonal, cosmetic grade)	40
	colorless (cubic)	15
bond length	hexagonal: 1.466 Å (with interlayer spacing of 3.331 Å)	41
	cubic: 1.56 Å	15
melting point	2973 °C; sublimes (hexagonal)	15
mean particle size	1-47 μm (varies by trade name and grade)	4,6,9-14
	30 μm (spherical morphology)	7
density	2.18 g/cm ³	39
	2.26 g/cm ³ (hexagonal, cosmetic-grade)	6
surface area	0.82-30 m ² /g (hexagonal; varies by grade)	4,6,9-12
	4 m ² /g (spherical morphology)	7
refractive index	1.74 (hexagonal)	6
solubility	insoluble in water and in acid solutions	39
stability	chemically inert and stable (hexagonal)	6
hardness	1-2 on the Mohs scale (hexagonal)	8
coefficient of friction	<0.3	6

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

	<i># of Uses</i> ¹⁷	<i>Max. Concentrations of Use (%)</i> ¹⁸
Totals*	643	0.01-25
Duration of Use		
<i>Leave-On</i>	641	0.01-25
<i>Rinse Off</i>	2	0.05
<i>Diluted for (Bath) Use</i>	NR	NR
Exposure Type		
Eye Area	320	0.08-25
Incidental Ingestion	3	2
Incidental Inhalation - Spray	12 ^a	0.8-0.9
Incidental Inhalation - Powder	103	1-16
Dermal Contact	636	0.01-25
Deodorant (underarm)	NR	NR
Hair - Non-Coloring	4	0.05
Hair-Coloring	NR	NR
Nail	2	2
Mucous Membrane	3	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

Table 3. Human repeated insult patch tests

Test Article	Conc. tested	No. of Subjects	Induction	Challenge	Results	Reference
eye shadow containing 13% boron nitride	70% in squalane oil	55	- occlusive 24-h patches applied to the back 3x/wk for 3 wks - 0.1-0.15 g of the test material (dose of 25-39 mg/cm ²) per patch - test sites were examined 24-48 h after patch removal	- the patch was applied to a previously unpatched site - the site was scored immediately and 48 h after patch removal	not an irritant or sensitizer no reactions were observed at any time	³²
pressed powder containing 16% boron nitride	applied neat	107	- 20 mg of the test article was distributed evenly over the surface of an 8 mm filter paper - Finn chambers were used - 48-72 h patches were applied to the back 3x/wk for 3 wks - test sites were examined 15-20 min after patch removal	- concurrent 48-h challenge applications were made to the induction site and to a previously unpatched site - the sites were examined daily for 3 days upon patch removal	not an irritant or sensitizer no adverse effects were observed during induction or challenge	³⁴
face powder containing 16% boron nitride	applied neat	104	- as described above	- as described above, with the exception that the sites were examined 30 min and 48 h after patch removal	not an irritant or a sensitizer no adverse effects were observed during induction or challenge	³⁵
eye shadow containing 18.7% boron nitride	applied neat	55	- occlusive 24-h patches applied to the back 3x/wk for 3 wks - amount applied was not stated - test sites were examined 24-48 h after patch removal	- the challenge patch was applied to a previously unpatched site - the test sites were evaluated immediately and 24 h and 48 h after patch removal	not an irritant or sensitizer no reactions were elicited during induction of challenge	³³

*the challenge followed a 2-wk non-treatment period in each study

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