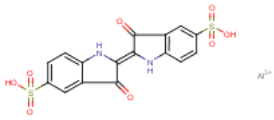
Pigment Blue 63

Ingredient synonym names

(delta2,2-Biindoline)-5,5'-disulfonic acid, 3,3'-dioxo-,aluminum salt
Acid Blue 74-aluminum lake
Aluminum 3,3'-dioxo-(delta2,2-biindoline)-5,5'disulfonate
Aluminum, 2-(1,3-dihydro-3-oxo-5-sulfo-2H-indol-2-ylidene)-2,3-dihydro-3-oxo-1H-indole-5-sulfonic acid complex
C.I. 73015 Aluminum lake
C.I. 73015-Aluminum lake
C.I. Acid Blue 74-aluminum lake
C.I. Food Blue 1-aluminum lake
C.I. Food Blue 1:1
C.I. Pigment Blue 63
Certolake indigo carmine
Food Blue No. 2-aluminum lake
Indigo carmine-aluminum lake
Indigotine-aluminum lake
Japan Blue 2 Aluminum lake
Japan Food Blue No. 2 aluminum lake
Pigment Blue 63

IDENTIFIER DETAILS

Ingredient chemical structure



CAS Number	FEMA Number	Additive Number
16521-38-3	-	E132 (sodium salt)

Ingredient EC Number	FL Number	CoE Number
240-589-3	-	-

Chemical formula: C16H10N2O8S2Al3+

Ingredient CLP Classification

Ingredient REACH Registration Number

No data identified

Acute Oral Toxicity	Eye Damage/Irritation	Carcinogenity
0	0	0

Acute Dermal Toxicity	Respiratory Sensitisation	Reproductive Toxicity
0	0	0

Acute Inhalation Toxicity	Skin Sensitisation	Aspiration Toxicity

Pigment Blue 63

0	0	0
Skin Corrosive/Irritant	Mutagenicity/ Genotoxicity	Specific Target Organ Toxicity
0	0	0

SPECIFICATIONS

Melting Point	> 250 ºC	Boiling Point	-

STATUS IN FOOD AND DRUG LAWS

Acceptable Daily Intake (ADI, mg/kg)	0-5 mg/kg bw
Acceptable Daily Intake (ADI) comments	Indigotine (sodium salt) - JECFA (1974)
FDA Status	176.180: Components of paper and paperboard in contact with dry food

CoE limits - Beverages (mg/kg)	-	CoE limits - Food (mg/kg)	-	CoE limits - Exceptions (mg/kg)	-

HUMAN EXPOSURE

Ingredient Natural Occurence (if applicable)

Indigo carmine is synthetically made

References - Ingredient Natural Occurence

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Ingredient Reported Uses

It is used as a colorant in beverages, chewing gum, drinks, frozen products and sunscreen. Its biological applications include treatment for amyloidosis, uses in medical devices and drug delivery systems. Indigo carmine also has industrial applications that include colour filters, toners, lithographic printing plates and toys (Sabnis, 2010).

References - Ingredient Reported Uses

Sabnis, (2010) Handbook of biological dyes and stains: Synthesis and industrial application

TOXICITY DATA

In Vivo Data

Acute Toxicity Data

Species	Test Type	Route Reported	Dosage

Mouse	LD50	Oral	2500 mg/kg
Mouse	LD50	Subcutaneous	405 mg/kg
Rat	LD50	intravenous	93 mg/kg
Rat	LD50	Oral	2000 mg/kg

(ChemIDplus, 2010)

In Vivo Carcinogenicity/Mutagenicity

Groups of 30 male and 30 female mice were fed diets containing 0.2, 0.4, 0.8 or l.16% indigo carmine (a food dye) for 80 wk. A group of 60 male and 60 female mice served as controls. The treatment had no effects on the death rate, body-weight gain, organ weights or the results of the histopathological examination, including the incidence of tumors. There was a slight anemia in mice given diets containing 0.8 or 1.6% indigo carmine. The feeding of indigo carmine to mice at dietary levels of up to 1.6% did not exert any carcinogenic effect. The no-untoward-effect level in this study was 0.4% of the diet (Hooson et al., 1975).

Groups of 60 male and 60 female rats were fed 0.5%, 1% or 2% indigo carmine in utero and for 29-30 months from weaning. Tumours were identified but were only present in the central nervous system. The author concludes that although a statistically significant increase in tumour number was found in the brain between high dose and mid, low-dose & control animals the tumours were spontaneous rather than chemically induced (Borzelleca et al., 1985a).

Charles River CD-1 mice were fed FD & C Blue No. 2 in the diet levels of 0.5, 1.5 and 5.0% in a long-term toxicity/carcinogenicity study. Maximum exposure was 23 months. No consistent compound-related or statistically significant biologically adverse effects were noted (Borzelleca et al., 1985b)

No evidence of carcinogenicity was obtained in various feeding studies conducted in both rats and mice (BIBRA, 1995)

In a two year study Hansen et al., (1966) exposed 80 rats to a weekly subcutaneous injection of 20 mg indigo carmine (2% aqueous solution). At the site of injection 14 rats developed malignant tumours. It is thought that sarcoma production was dependent on the physical properties of the injected material rather to any chemical carcinogenic properties (BIBRA, 1995)

Different concentrations of indigotine were evaluated for genotoxicity in the Somatic Mutation and Recombination Test (SMART) of Drosophila melanogaster. Standard cross was used in the experiment. Larvae including two linked recessive wing hair mutations were chronically fed at different concentrations of the test compounds in standard Drosophila Instant Medium. Feeding ended with pupation of the surviving larvae. Wings of the emerging adult flies were scored for the presence of spots of mutant cells which can result from either somatic mutation or somatic recombination. For the evaluation of genotoxic effects, the frequencies of spots per wing in the treated series were compared to the control group, which was distilled water. Indigotine demonstrated negative results. (Sarikaya, 2012)

References - In Vivo Carcinogenicity/Mutagenicity

Borzelleca JF, et al., (1985a) Chronic toxicity/carcinogenicity study of FD & C Blue No. 2 in rats. Food Chem Toxicol: 23(8):719-22.

Borzelleca JF, et al., (1985b) Chronic toxicity/carcinogenicity study of FD & C Blue No. 2 in mice. Food Chem Toxicol: 23(8):551-558.

Hansen, W. H. et al. (1966). Chronic toxicity of two food colors, brilliant blue FCF and indigotine. Toxicol. appl. Pharmacol: 8, 29

Hooson et al., (1975). Long-term toxicity of indigo carmine in mice. Food Cosmet Toxicol: 13 (2). 167-176 9.

Sarikaya et al (2012). Chemosphere. 2012 Aug;88(8):974-9. Epub 2012 Apr 4.

Dermal Toxicity

A concentration of 1% indigo carmine in petrolatum has been used in 48-hr covered patch tests to detect the sensitized state (Mancuso et al., 1990) and would thus be unlikely to irritate the skin of most normal individuals (BIBRA, 1995)

References - Dermal Toxicity

BIBRA toxicity profile: Indigo carmine, (1995).

Reproductive/ Developmental Toxicity

Borzelleca et al., (1987) exposed indigo carmine (25, 75 or 250 mg/kg bw/day) to groups of 20 female CD rats (6-15 days of pregnancy) and 10 female Dutch belted rabbits (6-18 days of pregnancy) by stomach tube. No treatment related developmental or teratogenic effects were seen in either species.

Within the same study mentioned previously ((Borzelleca et al., 1985a), the author had fed the rats 8 weeks before mating, throughout pregnancy and lactation and after weaning. No toxicological effects were observed on the pregnant females or pup viability at birth. Although pup mortality in the mid- and high dose groups was increased during days 12-19 of life and mean pup weight in all groups was reduced at the end of lactation, the author concludes that neither of these effects were statistically significant (BIBRA, 1995).

Mahadevan et al., (1993) compared the effect of methylene blue (MB) and Indigo carmine (IC) on human granulosa luteal cell (GC) function in vitro. MB significantly reduced progesterone production and was present as granules within the GC cells. IC did not appear to have any effect and was not observed within the cells.

References - Reproductive/ Developmental Toxicity

Borzelleca JF, et al., (1987). Evaluation of the potential teratogenicity of FD & C Blue No. 2 in rats and rabbits. Food Chem Toxicol: 25(7):495-7

BIBRA toxicity profile: Indigo carmine, (1995).

Mahadevan MM et al., (1993) Methylene blue but not indigo carmine is toxic to human luteal cells in vitro. Reprod Toxicol: 7(6):631-3

Inhalation Toxicity

No data identified

References - Inhalation Toxicity

No data identified

Cardiac Toxicity

No data identified

References - Cardiac Toxicity

No data identified

Addictive Data

No data identified

References - Addictive Data

No data identified

Behavioral data

No data identified

References - Behavioral data

No data identified

In Vivo - Other Relevant Studies

Groups of 25 male and 25 female mice received weekly for 104 weeks subcutaneous injections of 2.5 mg indigotine as a 1% aqueous solution, the control group of 50 receiving 0.25 ml physiological saline. Many mice died from acute convulsions immediately after injection of the test dye but otherwise no deleterious effects attributable to the subcutaneous injections were noted. Tumours were randomly distributed among test and control groups (Hansen et al., 1966).

In a 90 day feeding study Gaunt et al., (1969) gave pigs (three/sex/dose) 150, 450, or 1350 mg/kg bw/day indigo carmine in their diet. No treatment related change to body weight gain, organ weights or histopathology was identified by the author.

In a 2 year dog, feeding study Hansen et al., (1966) administered approx. 250 or 500 mg/kg bw/day indigo carmine to their daily diet. No treatment related differences to body weight gain, organ weights or histopathology between control and test groups was identified by the author.

Lethco et al., (1966) exposed rats to 35S-labelled indigotine by intravenous injection and orally. After intravenous injection 63% of the radioactivity appeared in the urine in six hours and 10% in the bile. The metabolites isatin-5-sulfuric acid and 5-sulfoanthranilic acid appeared in the urine after two hours. After oral administration, only 3% of the radioactivity appeared in urine in three days, suggesting poor absorption from the alimentary tract. Faeces contained 60-80 per cent.of the oral dose. The faecal content was due to lack of absorption, not biliary excretion (JECFA, 1975).

References - In Vivo - Other Relevant Studies

Gaunt, I. F. et al., (1969). Short-term toxicity study on indigo carmine in the pig. Fd. Cosmet. Toxicol :7(1), 17-24

Hansen, W. H. et al. (1966). Chronic toxicity of two food colors, brilliant blue FCF and indigotine. Toxicol. appl. Pharmacol: 8, 29

JECFA, (1975). Eighteenth Report of the Joint FAO/WHO Expert Committee on Food Additives.

In Vitro Data

In Vitro Carcinogenicity/Mutagenicity

The mutagencity of indigotine has been assessd in a large number of Ames assays using Salmonella typhimurium (TA98, TA100, TA1535, TA1537, TA1538) in the presence and absence of a rat liver metabolic activation system. No point mutations were induced in other bacterial tests using Escherichia coli and streptomyces coelicolor (BIBRA, 1995).

Indigo carmine did not induce chromosomal damage in human lymphocytes in the absence of metabolic activation. In the absence of metabolic activation, chromosome aberrations were not increased in Chinese hamster lung fibroblasts (Ishidate, et al., 1987). However there was evidence of polyploidy. In the presence of a metabolic activation system chromosome aberrations were increased but the extent of the increase was not stated (BIBRA, 1995)

Cameron et al., (1987) states that indigo carmine did not induce mutagenic effects in mouse lymphoma cells in the absence of a rat liver metabolic activation system. However, in the presence of the metabolic activation system a treatment but not dose related statistically significant mutation frequency was observed.

There was no evidence of genotoxic activity in bacterial rec-assays using Bacillus subtilis either in the absence or presence of a liver metabolic activation system in various studies (BIBRA, 1995).

References - In Vitro Carcinogenicity/Mutagenicity

BIBRA toxicity profile: Indigo carmine, (1995).

In Vitro - Other Relevant Studies

No data identified

References - In Vitro - Other Relevant Studies

No data identified

Emissions and Associated Toxicity Data

No data identified

References - Emissions and Associated Toxicity Data

No data identified