DISPERSE BLUE 1

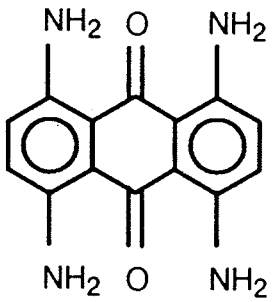
1. Chemical and Physical Data

Disperse Blue 1 is produced and used as a mixture of chemicals (see section 1.4). Sections 1.1-1.3 give the chemical and physical characteristics of the principal colour component or of the dye.

1.1 Synonyms

Chem. Abstr. Services Reg. No.: 2475-45-8
Chem. Abstr. Name: 9,10-Anthracenedione, 1,4,5,8-tetraamino-
IUPAC Systematic Name: 1,4,5,8-Tetraaminoanthraquinone
Colour Index No.: 64500
Synonyms: CI Disperse Blue 1; CI Solvent Blue 18; 1,4,5,8-tetraaminoanthraquinone

1.2 Structural and molecular formulae and molecular weight of 1,4,5,8-tetraaminoanthraquinone



$C_{14}H_{12}N_4O_2$ Mol. wt: 268.28

1.3 Chemical and physical properties of Disperse Blue 1

(*a*) *Description*: Blue-black microcrystalline powder (National Toxicology Program, 1986)

(*b*) *Melting-point*: 332°C (National Toxicology Program, 1986); >285°C (Nishida *et al.*, 1977)

(*c*) *Spectroscopy data*: Infrared, ultraviolet and nuclear magnetic resonance spectral data have been reported (National Toxicology Program, 1986); infrared (prism [1477B]; prism-FT [1018A]) spectral data have also been reported by Pouchert (1981, 1985).

(*d*) *Solubility*: Very slightly soluble in water (30 μg/l at 25°C; Kuroiwa & Ogasawara, 1973); soluble in acetone, ethanol and cellosolve; slightly soluble in benzene and linseed oil (Enviro Control, 1981)

(*e*) *Volatility*: Vapour pressure, 1.37×10^{-5} mm Hg [calculated by the Working Group] (Nishida *et al.*, 1977)

(*f*) *Stability*: Degrades at > -20°C (National Toxicology Program, 1986)

(*g*) *Octanol/water partition coefficient (P)*: log P = -0.96 (Baughman & Perenich, 1988)

1.4 Technical products and impurities

Trade Names: Acetate Blue G; Acetoquinone Blue L; Acetoquinone Blue R; Acetylon Fast Blue G; Amacel Blue GG; Amacel Pure Blue B; Artisil Blue SAP; Artisil Blue SAP Conc; Brasilazet Blue GR; Celanthrene Pure Blue BRS; Celliton Blue BB; Celliton Blue BB-CF; Celliton Blue Extra; Celliton Blue G; Celliton Blue GA; Celliton Blue GA-CF; Cibacet Blue 2GS; Cibacet Sapphire Blue G; Cilla Blue Extra; Diacelliton Fast Blue R; Dianix Blue QTA; Disperse Fast Blue BR; Duranol Brilliant Blue CB; Durosperse Blue CTP; Fenacet Blue G; Fenacet Blue GE; Grasol Blue 2GS; Hisperse Blue PRB; Intrasperse Printing Blue 2B; Intrasperse Sapphire Blue G; Kayalon Fast Blue BR; Microsetile Blue EB; Miketon Fast Blue; Miketon Fast Blue B; Nacelan Blue G; Navicet Blue Extra; Neosetile Blue EB; Nyloquinone Blue 2J; Oracet Sapphire Blue G; Palacet Blue Extra; Pamacel Pure Blue B-I; Perliton Blue B; Serinyl Blue 2G; Serinyl Blue 3G; Serinyl Blue 3GN; Setacyl Blue 2GS; Setacyl Blue 2GS II; Solvent Blue 18; Supracet Brilliant Blue 2GN; Supracet Deep Blue R

Commercial preparations of Disperse Blue 1 (approximately 50% 1,4,5,8-tetraaminoanthraquinone, 30% structurally related compounds and 20% water) contain approximately equal amounts of dyestuff and lignosulfonate dispersants (Burnett & Squire, 1986; National Toxicology Program, 1986). One US distributor markets Disperse Blue 1 with a dye content of approximately 30% (Aldrich Chemical Co., 1988).

2. Production, Use, Occurrence and Analysis

2.1 Production and use

(*a*) *Production*

Disperse Blue 1 has been prepared by acylation of 1,5-diaminoanthraquinone with oxalic acid, then nitration in sulfuric acid, followed by hydrolysis and reduction to the tetraamino compound; and by the reduction of mixed 1,5- and 1,8-dinitroanthraquinone to the corre-

sponding diamino compounds, followed by acetylation, nitration, reduction and hydrolysis (Society of Dyers and Colourists, 1971).

US production of Disperse Blue 1 was reported to be 159 tonnes in 1972 (US Tariff Commission, 1974). Separate figures were not reported after 1972, but production of all Disperse Blue dyes was approximately 6030, 9940 and 5740 tonnes in 1975, 1980 and 1985, respectively (US International Trade Commission, 1977, 1981, 1986). Disperse Blue 1 is no longer produced in the USA, but approximately 4-6 tonnes of the material are imported annually (National Toxicology Program, 1986).

No information on production of this dye in other countries was available to the Working Group.

(*b*) *Use*

Disperse Blue 1 is used in the USA in semipermanent hair colour formulations (see IARC, 1982) at concentrations of less than 1%. The solubility of the material in these preparations (approximately 500 ppm [mg/l]) is considerably greater than its solubility in water (National Toxicology Program, 1986).

Disperse Blue 1 has been used as a fabric dye for nylon, cellulose acetate and triacetate, polyester and acrylate fibres. It has also been used for surface dyeing of thermoplastics and as a solvent dye in cellulose acetate plastics (Enviro Control, 1981).

(*c*) *Regulatory status and guidelines*

No regulatory standard or guideline has been established for Disperse Blue 1.

2.2 Occurrence

(*a*) *Natural occurrence*

Disperse Blue 1 is not known to occur as a natural product.

(*b*) *Occupational exposure*

No data were available to the Working Group on exposure levels in the workplace; however, since Disperse Blue 1 is used in hair dyes, dermal and inhalation exposures may occur among people producing and applying such products.

2.3 Analysis

A method has been described for the spectrophotometric determination of Disperse Blue 1 sorbed on polyethylene terephthalate fibres by dye extraction in mixed solvent systems (Madan & Khan, 1978). A polarographic method for the determination of aminoanthraquinones, including 1,4,5,8-tetraaminoanthraquinone, in environmental and biological samples can be used to determine concentrations as low as 0.1-0.5 mg/ml (Popescu & Barbacaru, 1985).

3. Biological Data Relevant to the Evaluation of Carcinogenic Risk to Humans

3.1 Carcinogenicity studies in animals

Oral administration

Mouse: Groups of 50 male and 50 female B6C3F$_1$ mice, seven weeks of age, were fed diets containing 0, 600, 1200 or 2500 ppm (mg/kg) diet Disperse Blue 1 (commercial grade without lignosulfonate dispersants, containing approximately 50% 1,4,5,8-tetraaminoanthraquinone, 19.5% water and ~30% other impurities, mainly an isomer of tetraaminoanthraquinone and a nitrotriaminoanthraquinone isomer) for 104 weeks to give doses in mg/kg bw per day of 0, 112, 239 and 540 in males and 0, 108, 235 and 520 in females. All animals were killed at 112-113 weeks of age. A significant trend to lower survival in higher dose males was observed when early deaths were excluded. The combined incidences of hepatocellular adenomas and carcinomas were increased in treated males (control, 9/50; low-dose, 21/50; mid-dose, 20/50; high dose, 16/50) and in low-dose females (control, 3/50; low-dose, 13/49; mid-dose, 3/50; high-dose, 4/50). Group incidences did not indicate a dose-response effect, and survival-adjusted trends were not significant. The observed incidences of alveolar/bronchiolar adenomas and carcinomas in male mice were 4/50 in controls, 9/49 in low-dose animals, 5/50 in mid-dose animals and 11/50 in high-dose animals. When adjusted for survival, the increase was dose-related (p = 0.018, incidental tumour test for trend; adjusted rates, 15.0, 27.2, 13.9 and 49.3%, respectively). A high incidence of urinary bladder calculi was observed in mice of each sex. High-dose males and females also had a high incidence of transitional-cell hyperplasia of the bladder (National Toxicology Program, 1986).

Rat: Groups of 50 male and 50 female Fischer 344/N rats, seven weeks of age, were fed diets containing 0, 1250, 2500 or 5000 ppm (mg/kg) diet Disperse Blue 1 (same grade as above) for 103 weeks to give doses in mg/kg bw per day of 0, 45, 95 and 217 in males and 0, 56, 111 and 240 in females. All animals were killed at 111-112 weeks of age. Survival in high-dose males and females and in mid-dose males was significantly reduced. Dose-related increases in the combined incidences of squamous-cell papillomas and carcinomas, transitional-cell papillomas and carcinomas, and leiomyomas and leiomyosarcomas of the bladder were observed in males and females. In addition, urinary bladder calculi were observed in the groups of rats in which the incidence of bladder tumours was increased (see Table 1). A dose-related increase in the incidence of pancreatic islet-cell adenomas and carcinomas combined was seen in males: control, 1/49; low-dose, 2/50; mid-dose, 5/50; high-dose, 3/50 (p = 0.042, incidental tumour test for trend; National Toxicology Program, 1986).

Table 1. Incidence of urinary bladder lesions in rats fed Disperse Blue 1[a]

Urinary bladder lesion	Dose group				Incidental tumour test for trend
	Control	1250 ppm	2500 ppm	5000 ppm	
Males					
Squamous-cell papillomas and carcinomas	0/49	0/50	2/50	4/49	$p = 0.02$
Transitional-cell papillomas and carcinomas	0/49	0/50	10/50	11/49	$p = 0.001$
Leiomyomas and leiomyosarcomas	0/49	0/50	7/50	41/49	$p < 0.001$
Calculi (gross)	0/49	0/50	16/50	21/49	
Females					
Squamous-cell papillomas and carcinomas	0/48	0/50	1/50	11/48	$p < 0.001$
Transitional-cell papillomas and carcinomas	0/48	0/50	15/50	21/48	$p < 0.001$
Leiomyomas and leiomyosarcomas	0/48	0/50	3/50	26/48	$p < 0.001$
Calculi (gross)	0/48	0/50	12/50	37/48	

[a]From National Toxicology Program (1986)

3.2 Other relevant biological data

(*a*) *Experimental systems*

(i) *Absorption, distribution, excretion and metabolism*

No data were available to the Working Group.

(ii) *Toxic effects*

The oral LD_{50} value for various dyes, including Disperse Blue 1, in rats ranged from 1.2 to >6.3 g/kg bw (Wernick *et al.*, 1975).

Disperse Blue 1 (containing 50% lignosulfonate dispersants) was administered to Fischer 344 rats in two short-term and one long-term studies. In one short-term study, it was given either by gavage at 1 g/kg bw for one to three days or in the diet at 1% for four days, and rats were killed the following day. In the second short-term study, it was given for four days, both orally by gavage at 1 g/kg bw and at dietary levels of 0.5% commercial dye or 0.25% and 0.5% dye without dispersants. In the long-term study, the dye was administered to rats at dietary levels of 0, 0.01, 0.10 and 1.0% for up to 19 months; interim sacrifices were made for tritiated thymidine autoradiography of the bladder and examination of the principal body organs. Administration by gavage resulted in accumulation of the dye within the renal tubules and nephropathy within three days. Dietary dosing with 1% resulted in low-grade hyperplasia of the bladder urothelium, epithelial erosion, with adhesion of dye particles, and submucosal oedema after four days. At weeks 5, 9 and 17, there was increased DNA synthesis in the urothelium of high-dose rats but no increased labelling in any other group. Bladder

lesions were seen only at the 1% level; epithelial erosion with adhering dye particles was seen by day 4, calculi and hyperplasia by week 5 and squamous metaplasia by week 9. The calculi contained more dye in males than in females and more calcium in females than in males. By month 6, dye particles were embedded in the bladder wall, with some evidence of histiocyte accumulation in their vicinity (Burnett & Squire, 1986).

Disperse Blue 1 was administered to Fischer 344/N rats and B6C3F$_1$ mice by oral administration in the diet for 14 days, 13 weeks or two years. In the 14-day studies, 2/5 female rats died after receiving 50 000 ppm [mg/kg], and all mice receiving 25 000 ppm or more died. In the 13-week studies, diets containing concentrations up to 20 000 and 10 000 ppm were fed to rats and mice, respectively. No compound-related death occurred in rats, but deaths occurred with 10 000 ppm in mice of each sex. Pathological changes that occurred in rats and mice given diets containing 2500 ppm or more included urinary tract calculi, urinary bladder inflammation, hyperplasia of the urinary bladder transitional epithelium and nephrosis. In the two-year studies (see also section 3.1), lesions related to treatment in rats included renal and urinary bladder calculi, renal casts, hydronephrosis and renal degeneration, renal and urinary bladder epithelial hyperplasia, urinary bladder squamous metaplasia and pigmentation of the urinary bladder and kidney. Lesions in mice that were considered to be related to treatment were inflammation, epithelial hyperplasia, calculi and fibrosis in the urinary bladder, casts in the renal tubular lumina and renal tubular degeneration (National Toxicology Program, 1986).

(iii) *Effects on reproduction and prenatal toxicity*

Oral administration of a commercial product (a composite of dyes and base components found in semipermanent hair dyes) containing 0.61% Disperse Blue 1 among other dyes had no effect on fertility, gestation, lactation or viability indices in rats and induced no teratogenicity in rats or rabbits (Wernick *et al.*, 1975).

(iv) *Genetic and related effects*

Disperse Blue was weakly mutagenic to *Salmonella typhimurium* TA1537, in the presence and absence of an exogenous metabolic system from Aroclor 1254-induced rat liver; it was not mutagenic to several other strains (Brown & Brown, 1976). In liquid preincubation asssays, it was mutagenic to TA1535, TA97 and TA98 (National Toxicology Program, 1986).

(*b*) *Humans*

No data were available to the Working Group.

3.3 Case reports and epidemiological studies of carcinogenicity to humans

No data were available to the Working Group.

4. Summary of Data Reported and Evaluation

4.1 Exposure data

Disperse Blue 1 is an aminoanthraquinone-based dyestuff used in hair colour formulations and in colouring fabrics and plastics. No data on occupational exposure levels were available.

4.2 Experimental carcinogenicity data

Disperse Blue 1 was tested for carcinogenicity by oral administration in one strain of mice and in one strain of rats. In mice, it produced an increase in the incidence of alveolar/bronchiolar adenomas and carcinomas (combined) and a marginal increase in the incidence of hepatocellular tumours in treated males. In rats of each sex, it produced transitional-cell papillomas and carcinomas, squamous-cell papillomas and carcinomas, and leiomyomas and leiomyosarcomas of the urinary bladder; in addition, urinary bladder calculi were observed in the groups of rats in which the incidence of urinary bladder neoplasms was increased. In male rats, the incidence of islet-cell adenomas and carcinomas of the pancreas was marginally increased.

4.3 Human carcinogenicity data

No data were available to the Working Group.

4.4 Other relevant data

Calculi were observed in the urinary tract of rats and mice given Disperse Blue 1 in the diet. Urinary bladder lesions included epithelial hyperplasia in rats and mice and squamous metaplasia in rats. Hyperplasia of the transitional epithelium of the renal pelvis occurred in rats.

Disperse Blue 1 was mutagenic to bacteria in the presence and absence of an exogenous metabolic system.

4.5 Evaluation[1]

There is *sufficient evidence* for the carcinogenicity of Disperse Blue 1 in experimental animals.

No data were available from studies in humans on the carcinogenicity of Disperse Blue 1.

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[1]For description of the italicized terms and criteria for making the evaluation, see Preamble, pp. 25-29.

Summary table of genetic and related effects of Disperse Blue 1

Nonmammalian systems													**Mammalian systems**																											
Prokaryotes		Lower eukaryotes				Plants			Insects				*In vitro*												*In vivo*															
													Animal cells								Human cells								Animals							Humans				
D	G	D	R	G	A	D	G	C	R	G	C	A	D	G	S	M	C	A	T	I	D	G	S	M	C	A	T	I	D	G	S	M	C	DL	A	D	S	M	C	A
	+																																						

A, aneuploidy; C, chromosomal aberrations; D, DNA damage; DL, dominant lethal mutation; G, gene mutation; I, inhibition of intercellular communication; M, micronuclei; R, mitotic recombination and gene conversion; S, sister chromatid exchange; T, cell transformation

In completing the table, the following symbol indicates the consensus of the Working Group with regard to the results for each endpoint:

\+ considered to be positive for the specific endpoint and level of biological complexity

Overall evaluation

Disperse Blue 1 is *possibly carcinogenic to humans (Group 2B).*

5. References

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