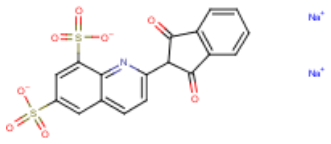
QUINOLINE YELLOW

SYNONYMS

Acid yellow 3
C.I. Acid Yellow 3
D & C Yellow no. 10
Quinoline Yellow
Quinoline yellow WS
2-(2-Quinolyl)-1,3-indandione disulfonic acid disodium salt
Disodium 2-(1,3-dioxo-2-indanyl)-6,8-quinolinesulphates
Disodium 2-(2-quinolyl)-indan-1,3-dionesulphonates
Basacid Yellow 094
Chinogelb Extra
Chinogelb wasserloeslich
E 104
FD and C Yellow No. 10
Food Yellow 13
Japan Yellow 203
Lemon Yellow ZN 3
Quinidine Yellow KT
Quinoline Yellow
Quinoline Yellow Extra
Quinoline Yellow S
Vitasyn Quinoline Yellow 70

CHEMICAL STRUCTURE



CHEMICAL FORMULA

$C_{18}H_9NO_8S_2.2Na$

IDENTIFIER DETAILS

CAS Number	:	8004-92-0 (Aluminium Lake CAS: 100208-62-6)
CoE Number	:	-
FEMA	:	-
EINECS Number	:	305-879-5
E Number	:	E104

SPECIFICATIONS

Melting Point: 150°C (decomposes)

Boiling point: -

STATUS IN FOOD, TOBACCO AND DRUG LAWS

CoE limits:

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

Acceptable Daily Intake:

ADI (mg/kg)	ADI Set by	Date Set	Comments
0 – 10 mg/kg	JECFA	1984	Latest evaluation
10 mg/kg	SCF	1983	Used same study as JECFA for evaluation
10 mg/kg	FDA		

FDA Status [CFR 21]:

Section Number	Comments
74.1710	Listing of colour additives subject to certification The colour additive D&C yellow No. 10 may be safely used for colouring drugs generally in amounts consistent with current good manufacturing practice.

HUMAN EXPOSURE

Natural Occurrence: Not found in nature

Reported Uses: Food colourant

Sources other than foods*:* Cosmetics and liquors

TOXICITY DATA

***In Vivo* Toxicity Status**

Species	Test	Route	Dose
Rat	LD_{50}	oral	2 gm/kg
Rat	LD_{50}	oral	5 gm/kg
Rat	LD_{50}	oral	2 gm/kg
Dog	LD_{50}	oral	1 gm/kg [SCF, 2004]

Cats were orally administered with 100 mg/kg bw quinoline yellow for 7 days. There was no effect on red blood cells [SCF, 2004].

Rats (5 males and 5 female) were fed quinoline yellow in the diet at 0.25, 0.5, 1.0, 2.0 and 5.0 % for 90 days. There were no adverse effects on body weight, food consumption, haematology or organ weights [BIBRA, 1990].

Out of 121 patients with the recurrent skin complaint, urticaria, 7 of these showed flare-up reactions when given 6 – 17 mg Quinoline Yellow (purity unspecified) orally over 3 h. Similarly, 5/62 children diagnosed as atopic [sensitised to many disparate chemicals] developed itching and/or reddening of the skin or urticarial rashes following oral ingestion of mixtures of food dyes including 1 or 10 mg Quinoline Yellow (purity not specified) [BIBRA, 1990].

An unpublished study reported no adverse effects on growth, behaviour or appearance in a group of 20 female and 20 male rats exposed to 3 % Quinoline Yellow in the diet. Blood and urinary parameters and gross and microscopic appearances were within normal limits [BIBRA, 1990].

Rats exposed *in utero* to Quinoline Yellow (70/sex/group) and then maintained on diets containing 0.03, 0.1, 0.5, 2.0 or 5.0 % for up to 30 months showed a decrease in body weight at the two highest dose levels and changes in the weights of the kidneys, adrenals, spleen, thyroid, uterus and ovaries, but with no evidence of tissue damage. No treatment-related effects were described at 0.5 % (250 mg/kg bw/day) [BIBRA, 1990].

Mice were exposed *in utero* to Quinoline Yellow (50/sex/group) and which had been subsequently maintained on diets containing 3 % Quinoline Yellow (1000 – 3300 mg/kg bw/day) for 21 – 23 months exhibited no conclusive evidence of toxicity. There was a slight decrease in white blood cell count in females at the highest dose and a slightly increased incidence of abdominal swellings was noted in all groups [BIBRA, 1990].

Mice (60/sex/group) fed up to 5 % Quinoline Yellow (7500 mg/kg bw/day) in the diet for 23 – 24 months displayed no adverse toxic effects. Abdominal swelling was present in all treatment groups including the controls [BIBRA, 1990].

No effects on body weight, food consumption and the microscopic appearance of an unspecified range of tissues were apparently seen in dogs (3/sex/group) fed dietary levels of 0.03 or 0.2 % (10 or 70 mg/kg bw/day) for 2 years [BIBRA, 1990].

Administration of 55 subcutaneous 1 ml injections of 2 % Qunioline Yellow (50 mg/kg bw) to rats (10/sex/group) over 7 months did not result in any adverse effects on behaviour, growth or survival throughout the animals' lifespan or affect microscopic appearance of the major organs [BIBRA, 1990].

Carcinogenicity and Mutagenicity

Mice (50/sex/group) were exposed *in utero* to Quinoline Yellow and then fed diets containing up to 3 % (1000 – 3300 mg/kg bw/day) for 21 – 23 months. There was no indication of carcinogenic activity [BIBRA, 1990].

Mice (60/sex/group) and rats (70/sex/group) were fed Quinoline Yellow in the diet for up to 30 months (approximately 7500 mg/kg bw/day for mice and 2500 mg/kg bw/day for rats). There was no evidence for carcinogenic activity. Rats had also been exposed to Quinoline Yellow *in utero* [BIBRA, 1990].

Dermal Toxicity

Human volunteers (15) were exposed to five 48 h covered skin applications over 2 weeks of 1 % Quinoline Yellow in water, on sites pre-treated with an irritant. No local reactions occurred when challenged with a 5 % solution, after a ten day rest period [BIBRA, 1990].

No sensitisation reactions were induced in 308 human volunteers exposed to nine 24 h covered skin applications of 1 % Quinoline Yellow in either petroleum or aqueous soap over 3 weeks, when they were challenged 2 weeks after the induction period with 1 %. Skin reactions were also absent when groups of up to 104 volunteers were subjected to a similar regime at lower concentrations of 0.005 - 0.1 %. Under similar experimental conditions as low as 10 ppm (0,001 %) D&C Yellow No.11 induced delayed sensitivity reactions in volunteers [BIBRA, 1990].

A patient who had been sensitised to D&C Yellow No.11 (0.0001 ppm in ethanol in 48 h covered patch tests) also reacted to aqueous Quinoline Yellow in a 48 h covered patch test at 50 ppm. No response was seen at 10 ppm. The volunteer also reacted to 200 ppm purified Quinoline Yellow (free from contaminating D&C Yellow No. 11) [BIBRA, 1990].

Human volunteers sensitised to D&C Yellow No.11, following repeated application of 0.5 % and reacting at challenge down to 0.01 % in petroleum, did not respond to 48 h covered contact with 5 % aqueous solutions of Quinolone Yellow (containing below 0.01 ppm D&C Yellow No. 11) [BIBRA, 1990].

Over a 5 year period a total of 11/365 of patients attending dermatitis clinics showed local reactions following patch testing (48 h covered contact) with a 1 % commercial sample of Quinoline Yellow in petroleum compared with 2/365 (0.5 %) tested with a purified sample at the same concentration. A further case of apparent sensitivity to Quinoline Yellow (purity unspecified) was seen in 1/7 cases tested with 0.5 % petroleum. It has been suggested that responses seen in patch tests with Quinoline Yellow may be due to cross-sensitivity between it and D&C Yellow No.11 or because of contaminating levels of D&C Yellow No.11 in Quinoline Yellow samples [BIBRA, 1990]

D & C Yellow No. 11 and Quinoline Yellow belong to a group of quinophtalone dyes with a common basic structure. D & C Yellow No. 11 is used mostly in plastics, spirit lacquers, coloured smokes and cosmetics, but it is also increasingly used as a dye in soaps and shampoos. Quinoline Yellow is used for dyeing wool, silk and nylon in cases where good light fastness is not required, but is most commonly used as a drug and food colouring agent. A patient, extremely sensitive to D & C Yellow No. 11 with a positive patch test reaction down to 0.00001%, also reacted to Quinoline Yellow at a test concentration of 0.1%. To establish if any cross-reactivity occurs between the two compounds, a high pressure liquid chromatograph was used for analysis, purification and separation of the two colours. The patient was then patch tested with the two colours and the pure fraction of Quinoline Yellow. The test results confirm a true sensitivity to Quinoline Yellow and to D & C Yellow No. 11, and may indicate cross-reactivity between the colours (Björkner et al., 1983).

There was no evidence of an allergic response in guinea-pigs challenged for 24 h with up to 10 % Quinoline Yellow under occlusion for 2 weeks after the end of an initiation phase (involved covered application of 40 % Quinoline Yellow to the skin for 24 h once a week for 3 weeks). Using a similar procedure (with an initiating concentration of 50 % in ethanol), D&C Yellow No.11 sensitised 11/13 animals tested [BIBRA, 1990].

Reproductive and Developmental Toxicity

Rats were fed Quinoline Yellow at up to 50 mg/kg bw/day in the diet two weeks prior to mating and then continuously through three successive generations. There was no compound-related effects on fertility, litter size, pup survival or pup weight [BIBRA, 1990].

Rats (60 male and 60 female) were exposed to 0.03, 0.1, 0.5, 2 or 5 % (2500 mg/kg bw/day) in the diet two months prior to mating and then continuously throughout pregnancy and lactation. Pups had a slightly reduced likelihood of survival and with slightly lower weight gains during lactation at dose levels of 0.5 % and above. No other reproductive effects were noted [BIBRA, 1990].

Rats fed 150 mg/kg bw/day from days 6 – 15 of pregnancy, or to rabbits from days 6 – 18 of pregnancy showed no signs of maternal or foetal toxicity or abnormalities [BIBRA, 1990].

The fertility and reproductive performance of mice (65/sex/group) were not affected when fed up to 3 % Quinoline Yellow in the diet (approximately 4500 mg/kg bw/day) for 9 weeks prior to mating and then throughout pregnancy [BIBRA, 1990].

Other relevant studies

There are two types of Quinoline Yellow commercially available as one of the benzene rings can be methylated. 2 (2-Quinolyl)-1,3-indandione, also known

as D&C Yellow No. 11, is often present in commercial Quinoline Yellow samples as a low level impurity, and both JECFA and the FDA have stipulated maximum levels of 4 ppm for this contaminant [BIBRA, 1990].

Metabolic studies in rats and dogs indicate that Quinoline Yellow is poorly absorbed from the gastrointestinal tract and is metabolised only to a limited extent. Only about 1 – 4 % of an oral dose was excreted in the urine in rats and dogs, with about 0.3 % of the total dose appearing as a water-soluble metabolite in the rat. Biliary excretion in rats accounted for about 1 % of an oral dose. Intravenous injections were rapidly cleared from the blood [BIBRA, 1990].

Quinoline Yellow has been reported to accumulate in the thyroid and ovary in the rat, but not in the dog [BIBRA, 1990].

The neurotoxic effects of four common food additives in combinations of two (Brilliant Blue and L-glutamic acid, Quinoline Yellow and aspartame) were examined to assess potential interactions. Mouse NB2a neuroblastoma cells were induced to differentiate and grow neurites in the presence of additives. Neurotoxicity was measured as an inhibition of neurite outgrowth. Two independent models were used to analyze combination effects: effect additivity and dose additivity. Significant synergy was observed between combinations of Brilliant Blue with L-glutamic acid, and Quinoline Yellow with aspartame, in both models. Involvement of N-methyl-D-aspartate (NMDA) receptors in food additive-induced neurite inhibition was assessed with a NMDA antagonist, CNS-1102. L-glutamic acid- and aspartame-induced neurotoxicity was reduced in the presence of CNS-1102; however, the antagonist did not prevent food colour-induced neurotoxicity. Theoretical exposure to additives was calculated based on analysis of content in foodstuff, and estimated percentage absorption from the gut. Inhibition of neurite outgrowth was found at concentrations of additives theoretically achievable in plasma by ingestion of a typical snack and drink. In addition, Trypan Blue dye exclusion was used to evaluate the cellular toxicity of food additives on cell viability of NB2a cells; both combinations had a straightforward additive effect on cytotoxicity. These data have implications for the cellular effects of common chemical entities ingested individually and in combination (Lau et al., 2006).

Behavioural Data

No data identified

In Vitro Toxicity Status

Carcinogenicity and Mutagenicity

Quinoline Yellow was not mutagenic in the Ames assay with or without metabolic activation, in *Salmonella typhimurium* (strain specified) and in *Escherichia coli* (strain not specified) [BIBRA, 1990].

Macioszek et al., in 2004 evaluated the mutagenic potential of quinoline yellow on two test systems; 1) human lymphocytes in vitro; 2) root tip meristem cells of *Vicia faba* in vivo, utilizing the micronucleus assay and the Comet assay in both test systems. In all experiments, lymphocytes and 4-day old seedlings of *Vicia faba* were treated with quinoline yellow solutions at three concentrations: 8.67, 86.7 and 867 µg/ml. The micronucleus test permits the detection of chromosomal breakage. The Comet assay allows the detection of nuclear DNA single- and double-strand breaks, and delayed or incomplete excision repair sites in the DNA of individual cells. Quninoline yellow was found to be clastogenic in the micronucleus assay in both test systems. These findings were confirmed by results of the Comet assay on root meristem cells. The mutagenic effect of quinoline yellow on human lymphocytes studied by means of the Comet assay, were only observed for its highest concentration, 867 µg/ml.

Other relevant studies

Quinoline yellow was shown to inhibit both true (acetyl) and pseudo (butyryl) cholinesterase (ChE) enzymes in human erthrocytes and plasma *in vitro*. A dose-dependent decrease in the activity of pseudo and true ChE activity of up to 53 % and 87 % respectively was reported. Blood cholinesterase inhibition greater than 20 % is generally considered to be adverse. The authors did not comment on the in vivo relevance of the concentrations tested [Osman et al., 2002].

The uptake, fate and excretion of quinoline yellow, a colouring in sweets and soft drinks, in the rat were studied. In the isolated perfused rat liver, 70% of the dose was excreted into the bile within 3 h. Similar results were obtained after intravenous injection into anaesthetised animals. When given by gavage, only approximately 1 % was excreted in bile and urine within 4 - 5 h. Quinoline yellow administered orally to rats was quantitatively excreted, the excretion being mainly faecal. Administration of quinoline yellow did not affect the activities of 2 microsomal enzymes, N-aminopyrine demethylase and aniline hydroxylase. Very little quinoline yellow is absorbed from the gastrointestinal tract of the rat. No evidence of metabolism was obtained (Wahlstrom et al., 1979).

Quinoline Yellow was not metabolised by an isolated rat liver preparation or by gut bacteria [BIBRA, 1990].

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