Pharmacopoeias. In *Chin.* and *Jpn.*
Eur. (see p.vii) includes Saffron for Homoeopathic Preparations.
Ph. Eur. 6.2 (Saffron for Homoeopathic Preparations). The dried stigmas of *Crocus sativus* usually joined by the base to a short style. It has a characteristic, aromatic odour. Protect from light.

Profile
Saffron consists of the dried stigmas and tops of the styles of *Crocus sativus* (Iridaceae), containing crocines, crocetins, and picrocrocine. Saffron is used to colour medicines, foods, and cosmetics. It is also used as a flavouring agent. Saffron has been included in preparations for teething pain. It is being investigated for the treatment of depression. There have been reports of poisoning with saffron, but in some cases these may have been due to meadow saffron, *Colchicum autumnale*.

Homoeopathy. Saffron has been used in homoeopathic medicines under the following names: Croci stigma; Crocus sativus; Crocus; Croc. s.

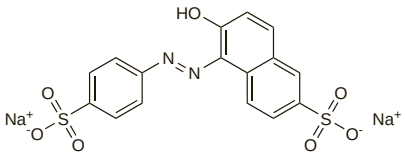
Preparations
Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Cz.:*** Dr Theiss Rheuma Creme†; Dr Theiss Schweden Krauter; Dr Theiss Schwedenbitter; ***Ger.:*** Infi-tract†; ***Rus.:*** Tentex (Тентекс); ***Spain:*** Dentol Topico; Dentomicin.

Sunset Yellow FCF
Amarillo anaranjado S; Amarillo ocaso FCF; CI Food Yellow 3; Colour Index No. 15985; Crelborange S; E110; FD & C Yellow No. 6; Günbatimi Sarisi FCF; Jaune Orangé S; Jaune Soleil; Orange Yellow S. Disodium 6-hydroxy-5-(4-sulphonatophenylazo)naphthalene-2-sulphonate.

Жёлтый Солнечный Закат

$C_{16}H_{10}N_2Na_2O_7S_2$ = 452.4.
CAS — 2783-94-0.



Profile
Sunset yellow FCF is used as a colouring agent in foods, medicines, and cosmetics. Sensitivity reactions have been reported.

Carcinogenicity. Although some evidence of carcinogenicity was found in early *animal* studies subsequent work failed to confirm these findings and in the UK sunset yellow FCF is considered suitable for use as a food colour.[1]

1. MAFF. Food advisory committee: final report on the review of the colouring matter in food regulations 1973. *FdAC/REP/4.* London. HMSO, 1987.

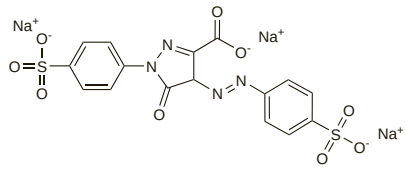
Hypersensitivity. Hypersensitivity reactions including severe abdominal cramps[1] and Quincke's oedema[2] have been recorded in individual patients receiving medication that was coloured with sunset yellow FCF.

1. Gross PA, *et al.* Additive allergy: allergic gastroenteritis due to yellow dye #6. *Ann Intern Med* 1989; **111:** 87–8.
2. Lévesque H, *et al.* Reporting adverse drug reactions by proprietary name. *Lancet* 1991; **338:** 393.

Tartrazine
CI Food Yellow 4; Colour Index No. 19140; E102; FD & C Yellow No. 5; Jaune Tartrique; Tartracina; Tartrazin.; Tartrazina; Tartrazol Yellow. It consists mainly of trisodium 5-hydroxy-1-(4-sulphonatophenyl)-4-(4-sulphonatophenylazo)pyrazole-3-carboxylate.

Тартразин

$C_{16}H_9N_4Na_3O_9S_2$ = 534.4.
CAS — 1934-21-0.



Profile
Tartrazine is used as a colouring agent in foods, cosmetics, and medicines. Some patients may experience sensitivity reactions.

Adverse Effects. There have been numerous reports of reactions to tartrazine including angioedema, asthma, urticaria, and anaphylactic shock. Some of the reports have dealt with cross-sensitivity, especially with aspirin, although the connection with aspirin has been questioned.[1] A suggested incidence[2] of tartrazine sensitivity is 1 in 10 000. The mechanism of the reactions may not necessarily be immunological.[3]

In considering the reports of tartrazine sensitivity or intolerance the Food Advisory Committee in the UK[1] reported that similar evidence of intolerance might well be obtained for a variety of natural food ingredients if as many studies were conducted on them as on tartrazine. The Committee considered that tartrazine posed no more problems than other colours or food ingredients and recommended that the continued use of tartrazine in food was acceptable. However, use of tartrazine in medicines appears to be diminishing.

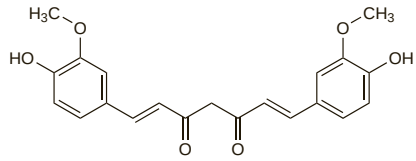
A systematic review[4] noted that there was no evidence that tartrazine makes asthma worse, nor did avoiding it make asthma any better.

Tartrazine has often been implicated in the aggravation of hyperactive behaviour in children; for a discussion, see Hyperactivity, p.1469.

1. MAFF. Food advisory committee: final report on the review of the colouring matter in food regulations 1973. *FdAC/REP/4.* London: HMSO, 1987.
2. Anonymous. Tartrazine: a yellow hazard. *Drug Ther Bull* 1980; **18:** 53–5.
3. Murdoch RD, *et al.* Tartrazine induced histamine release in vivo in normal subjects. *J R Coll Physicians Lond* 1987; **21:** 257–61.
4. Ram FS, Ardern KD. Tartrazine exclusion for allergic asthma. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2001 (accessed 18/04/07).

Turmeric
CI Natural Yellow 3; Cúrcuma; Indian Saffron.

Куркума; Турмерик
CAS — 458-37-7.



Pharmacopoeias. In *Chin.*

Profile
Turmeric, the dried rhizome of *Curcuma longa* (Zingiberaceae), is used principally as a constituent of curry powders and other condiments. Turmeric and its main ingredient curcumin (p.1471) are used as yellow colouring agents in foods. Turmeric has also been used as an ingredient of preparations indicated for biliary and gastrointestinal disorders and has been promoted as an anti-inflammatory. Turmeric is the source of turmeric oil. Turmeric is a commonly used ayurvedic medicine. Other species of *Curcuma* may be used similarly.

◊ Reviews of the properties of turmeric and curcumin.

1. Ammon HP, Wahl MA. Pharmacology of Curcuma longa. *Planta Med* 1991; **57:** 1–7.
2. Grant KL, Schneider CD. Turmeric. *Am J Health-Syst Pharm* 2000; **57:** 1121–2.
3. Ringman JM, *et al.* A potential role of the curry spice curcumin in Alzheimer's disease. *Curr Alzheimer Res* 2005; **2:** 131–6.
4. Singh S, Khar A. Biological effects of curcumin and its role in cancer chemoprevention and therapy. *Anticancer Agents Med Chem* 2006; **6:** 259–70.
5. Menon VP, Sudheer AR. Antioxidant and anti-inflammatory properties of curcumin. *Adv Exp Med Biol* 2007; **595:** 105–25.
6. Sharma RA, *et al.* Pharmacokinetics and pharmacodynamics of curcumin. *Adv Exp Med Biol* 2007; **595:** 453–70.
7. Strimpakos AS, Sharma RA. Curcumin: preventive and therapeutic properties in laboratory studies and clinical trials. *Antioxid Redox Signal* 2008; **10:** 511–45.
8. Hatcher H, *et al.* Curcumin: from ancient medicine to current clinical trials. *Cell Mol Life Sci* 2008; **65:** 1631–52.

Effects on the thyroid. There has been some concern about the safety of turmeric oleoresin, an extract of turmeric, after reports of adverse thyroid changes in *pigs*.[1,2]

1. MAFF. Food advisory committee: final report on the review of the colouring matter in food regulations 1973. *FdAC/REP/4.* London: HMSO, 1987.
2. FAO/WHO. Evaluation of certain food additives and contaminants: thirty-fifth report of the joint FAO/WHO expert committee on food additives. *WHO Tech Rep Ser 789* 1990. Also available at: http://libdoc.who.int/trs/WHO_TRS_789.pdf (accessed 30/05/07)

Preparations
Proprietary Preparations (details are given in Part 3)
Chile: Turmerik; ***Ger.:*** Aristochol CC†; Choldestal†; Sergast†; ***Indon.:*** Rheumakur; ***Pol.:*** Solaren.

Multi-ingredient: ***Austral.:*** Arthriforte; Bioglan Joint Mobility; Extralife Arthri-Care; Extralife Liva-Care; Herbal Digestive Formula†; Vitanox; ***Austria:*** Apozema; Spasmo Claim; ***Canad.:*** Milk Thistle; ***Cz.:*** Cholagol; ***Fr.:*** Hepatoum; ***Ger.:*** Chol-Arbuz NF; Cholagogum F†; Cholagogum N†; Cholosom Phyto N; Digest-Merz†; Gallo Merz N†; Gastrol S†; Hepaticum-Medice H†; Horvilan N; Opobyl-phyto†; spasmo gallo sanol†; Ventracid N; ***Hong Kong:*** Hepatofalk Planta; ***Hung.:*** Cholagol; ***India:*** FN-T-Tus; ***Indon.:*** Aptivium Liver Support; Diapet; Entrodiar; Fitodiar; Heparviton; Heparviton NF; Hepasil; Hepatin; Lanagogum; Lecur; Procur Plus; Reliv; Tripid; ***Ital.:*** Cinarepa; Reumafort; ***Mex.:*** Ifuchol; Rodan; ***Pol.:*** Chelicur; Cholitol; ***Rus.:*** Cholagol (Холагол); Doktor Mom (Доктор Мом); Suprima-Broncho (Суприма-бронхо); ***S.Afr.:*** Lewensessens; ***Singapore:*** Artrex†; ***Switz.:*** Stago N†; ***UK:*** Arheumacare; BackOsamine.

Vegetable Carbon
Bitkisel Kömür; Carbon Black; Carbón vegetal; E153; Vegetable Black.

Уголь Растительный

NOTE. The name Carbon Black has also been used as a synonym for Channel Black, a colouring agent not used in food; care should be taken to avoid confusion between the two compounds.

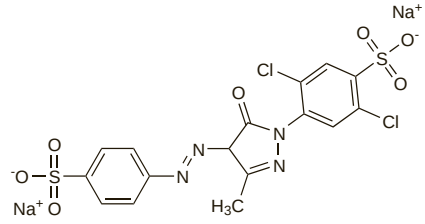
Profile
Vegetable carbon, which consists essentially of finely divided carbon, is produced by the carbonisation of vegetable material such as peat or wood. It is used as a colouring agent for medicines, foodstuffs, and cosmetics.

Preparations
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Chile:*** Kordinol Compuesto†; ***Fr.:*** Stomargil.

Yellow 2G
107; Acid Light Yellow 2G; Acid Yellow 17; Amarillo 2G; CI Food Yellow 5; Colour Index No. 18965. Disodium 2,5-dichloro-4-[5-hydroxy-3-methyl-4-(4-sulphonatophenylazo)pyrazol-1-yl]benzenesulphonate.

Жёлтый 2G

$C_{16}H_{10}Cl_2N_4Na_2O_7S_2$ = 551.3.
CAS — 6359-98-4.



Profile
Yellow 2G is used as a colouring agent in cosmetics.

Bronchography (examination of the bronchial tree) has been performed with oily or aqueous media, such as iopydol or iopydone, instilled through a catheter or bronchoscope to coat the airways; however, other visualisation techniques are generally preferred.

For **hysterosalpingography** (visualisation of the uterus and fallopian tubes) ultrasound and endoscopic techniques are generally used, and microbubble contrast media such as galactose may be used to improve ultrasound images. If radiography is performed, water-soluble iodinated contrast media may be used.

For **lymphography** or **lymphangiography** (visualisation of the lymphatic system) a high radiodensity is required and the contrast medium must be retained within the lymphatic system for long enough to be visualised, requiring particulate, water-insoluble media, or very large molecules. Iodised oil has been most widely used, but adverse effects and limited distribution within the lymphatic system restrict its use.

Adverse effects of contrast media. Although contrast media are generally considered to be very safe, with most adverse effects being mild and transient, more severe and even life-threatening reactions are possible, and the risk of adverse effects may influence the choice of contrast medium or imaging technique in a particular patient.

Iodinated radiographic contrast media all have a similar range of adverse effects (see under Amidotrizoic Acid, p.1475) but the incidence and severity varies. Many of the adverse effects are related to the osmolality of the preparation, and the incidence tends to be lower with those that have low osmolality. Osmolality depends on the number of particles present in the solution; for a given iodine content, this is highest for the ionic monomers and lowest for nonionic dimers, and this is reflected in the incidence of adverse effects. Hypersensitivity reactions also tend to be less frequent with nonionic media (see under Amidotrizoic Acid, p.1476), although these reactions are not directly related to osmolality. However, low-osmolality media tend to be more expensive; while nonionics and dimers are preferred, ionic monomers may still have a role in patients at low risk of adverse effects. Ionic contrast media may also carry a lower risk of thromboembolism (see Effects on the Blood, p.1476).

Magnetic resonance contrast media tend to be safer than iodinated contrast media, although similar general effects may occur. Ionic and nonionic media are available, but this tends to have little influence on the incidence of adverse effects. All gadolinium chelates have similar adverse effects (see under Gadopentetic Acid, p.1479); there is a theoretical risk of gadolinium toxicity due to instability of the chelates and most preparations also contain free chelating agent to reduce this risk. The adverse effects of superparamagnetic iron compounds are described under ferumoxides (p.1478) and ferumoxsil (p.1478).

Ultrasound contrast media are generally safe; minor and transient adverse effects have been reported, but may be due to the procedure rather than to the contrast medium used.

References.

1. Thomsen HS, Bush WH. Adverse effects of contrast media: incidence, prevention and management. *Drug Safety* 1998; **19:** 313–24.
2. Runge VM. Safety of approved MR contrast media for intravenous injection. *J Magn Reson Imaging* 2000; **12:** 205–13.
3. Maddox TG. Adverse reactions to contrast material: recognition, prevention, and treatment. *Am Fam Physician* 2002; **66:** 1229–34.
4. Kirchin MA, Runge VM. Contrast agents for magnetic resonance imaging: safety update. *Top Magn Reson Imaging* 2003; **14:** 426–35.
5. Christiansen C. X-ray contrast media—an overview. *Toxicology* 2005; **209:** 185–7.
6. Jakobsen JÅ, *et al.* Safety of ultrasound contrast agents. *Eur Radiol* 2005; **15:** 941–5.
7. Morcos SK. Acute serious and fatal reactions to contrast media: our current understanding. *Br J Radiol* 2005; **78:** 686–93.
8. Meth MJ, Maibach HI. Current understanding of contrast media reactions and implications for clinical management. *Drug Safety* 2006; **29:** 133–41.
9. European Society of Urogenital Radiology. ESUR guidelines on contrast media (February 2007). Available at: http://www.esur.org/fileadmin/Guidelines/ESUR_2007_Guideline_6_Kern_Ubersicht.pdf (accessed 14/07/08)

Adipiodone *(BAN, rINN)*

Adipiodon; Adipiodona; Adipiodoni; Adipiodonum; Iodipamide. 3,3′-Adipoyldiaminobis(2,4,6-tri-iodobenzoic acid).

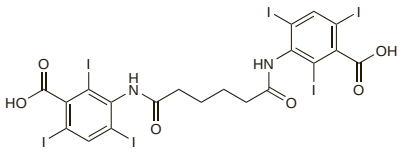
Адипиодон

$C_{20}H_{14}I_6N_2O_6$ = 1139.8.

CAS — 606-17-7.

ATC — V08AC04.

ATC Vet — QV08AC04.



Description. Adipiodone contains about 66.8% of I.

Pharmacopoeias. In *Chin.* and *US.*

USP 31 (Iodipamide). A white, practically odourless, crystalline powder. Very slightly soluble in water, in chloroform, and in ether; slightly soluble in alcohol. Store at a temperature of 25°, excursions permitted between 15° and 30°.

Meglumine Adipiodone *(rINNM)*

Adipiodona de meglumina; Adipiodone Méglumine; Adipiodone Meglumine *(BANM)*; Dimeglumine Iodipamide; Iodipamide Meglumine; Meglumine Iodipamide; Meglumini Adipiodonum. The di(*N*-methylglucamine) salt of adipiodone.

Меглумина Адипиодон

$C_{20}H_{14}I_6N_2O_6.(C_7H_{17}NO_5)_2$ = 1530.2.

CAS — 3521-84-4.

ATC — V08AC04.

ATC Vet — QV08AC04.

Description. Meglumine adipiodone contains about 49.8% of I.

Pharmacopoeias. *US* includes only as an injection.

Incompatibility. Incompatibilities have been reported between meglumine adipiodone and some antihistamines.

Adverse Effects, Treatment, and Precautions

See under the amidotrizoates, p.1475. Rapid injection may increase the incidence of adverse effects.

Adipiodone may show some uricosuric activity.

Effects on the liver. Of 149 patients given the recommended dose of adipiodone, 13 developed elevated serum aspartate aminotransferase (SGOT) values; of 126 who received twice the dose, 23 developed elevated values.[1] Hepatotoxicity has also been reported[2-4] on isolated occasions in patients given meglumine adipiodone.

1. Scholz FJ, *et al.* Hepatotoxicity in cholangiography. *JAMA* 1974; **229:** 1724.
2. Stillman AE. Hepatotoxic reaction to iodipamide meglumine injection. *JAMA* 1974; **228:** 1420–1.
3. Sutherland LR, *et al.* Meglumine iodipamide (Cholografin) hepatotoxicity. *Ann Intern Med* 1977; **86:** 437–9.
4. Imoto S. Meglumine hepatotoxicity. *Ann Intern Med* 1978; **88:** 129.

Pharmacokinetics

Meglumine adipiodone is rapidly distributed in extracellular fluid after intravenous injection and is reported to be extensively bound to plasma proteins. It appears in the bile ducts within about 10 to 15 minutes after injection, with peak opacity at about 20 to 30 minutes, and reaches the gallbladder by about 1 hour, peak opacification occurring after about 2 hours. About 80 to 95% is excreted unchanged in the faeces; small amounts are excreted unchanged in urine. A terminal half-life of about 2 hours has been reported.

Uses and Administration

Adipiodone is an ionic dimeric iodinated radiographic contrast medium (see p.1474); it is taken up by the liver and excreted in bile, and is used in cholangiography and cholecystography.

Adipiodone is given intravenously as a solution containing 52% of the meglumine salt. The usual dose is about 10 g of meglumine adipiodone, given by slow intravenous injection over about 10 minutes.

A solution of meglumine adipiodone with meglumine diatrizoate is given by intra-uterine instillation for hysterosalpingography.

Preparations

BP 2008: Meglumine Iodipamide Injection;
USP 31: Iodipamide Meglumine Injection.

Proprietary Preparations (details are given in Part 3)

USA: Cholografin.

Multi-ingredient: ***USA:*** Sinografin.

Amidotrizoic Acid *(BAN, rINNM)*

Acide amidotrizoïque; Ácido amidotrizoico; Acidum amidotrizoicum; Acidum Diatrizoicum; Amidotritsoiinihappo; Amidotrizoesav; Amidotrizoinė rūgštis; Amidotrizoinsyra; Diatritsoiinihappo; Diatrizoic Acid *(USAN)*; Diatrizoinsyra; Kyselina amidotrizoová; NSC-262168. 3,5-Diacetamido-2,4,6-tri-iodobenzoic acid.

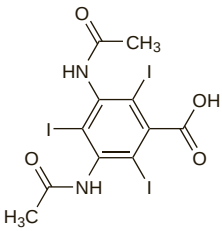
Амидотризоевая Кислота

$C_{11}H_9I_3N_2O_4.2H_2O$ = 649.9.

CAS — 117-96-4 (anhydrous amidotrizoic acid); 50978-11-5 (amidotrizoic acid dihydrate).

ATC — V08AA01.

ATC Vet — QV08AA01.



Description. Amidotrizoic acid contains about 62% of I calculated on the anhydrous substance.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US.*

Ph. Eur. 6.2 (Amidotrizoic Acid Dihydrate). A white or almost white, crystalline powder. Very slightly soluble in water and in alcohol; dissolves in dilute solutions of alkali hydroxides. Protect from light.

USP 31 (Diatrizoic Acid). It is anhydrous or contains two molecules of water of hydration. A white, odourless, powder. Very slightly soluble in water and in alcohol; soluble in dimethylformamide and in alkali hydroxide solutions.

Meglumine Amidotrizoate *(BANM, rINNM)*

Amidotrizoate de Méglumine; Amidotrizoato de meglumina; Diatrizoate Meglumine; Meglumine Diatrizoate; Meglumini Amidotrizoas; Methylglucamine Diatrizoate. *N*-Methylglucamine 3,5-diacetamido-2,4,6-tri-iodobenzoate.

Меглумина Амидотризоат

$C_{11}H_9I_3N_2O_4.C_7H_{17}NO_5$ = 809.1.

CAS — 131-49-7.

ATC — V08AA01.

ATC Vet — QV08AA01.

Description. Meglumine amidotrizoate contains about 47.1% of I.

Pharmacopoeias. In *US.*

USP 31 (Diatrizoate Meglumine). A white, odourless, powder. Freely soluble in water. Store at a temperature of 25°, excursions permitted between 15° and 30°.

Sodium Amidotrizoate *(BANM, rINN)*

Amidotrizoate de Sodium; Amidotrizoato de sodio; Diatrizoate Sodium; Natrii amidotrizoas; Natrio amidotrizoatas; Natriumamidotritsoaatti; Natriumamidotrizoat; Nátrium-amidotrizoát; Natrium-amidotrizoát; NSC-61815; Sodium, amidotrizoate de; Sodium Diatrizoate; Sodu amidotrizoat. Sodium 3,5-diacetamido-2,4,6-tri-iodobenzoate.

Натрия Амидотризоат

$C_{11}H_8I_3N_2NaO_4$ = 635.9.

CAS — 737-31-5.

ATC — V08AA01.

ATC Vet — QV08AA01.

Description. Sodium amidotrizoate contains about 59.9% of I calculated on the anhydrous substance.

Pharmacopoeias. In *Eur.* (see p.vii), *Int.*, and *US.*
Chin. includes the injection.

Ph. Eur. 6.2 (Sodium Amidotrizoate). A white or almost white powder. Freely soluble in water; slightly soluble in alcohol; practically insoluble in acetone. A 50% solution in water has a pH of 7.5 to 9.5. Protect from light.

USP 31 (Diatrizoate Sodium). A white, odourless, powder. Soluble in water; slightly soluble in alcohol; practically insoluble in acetone and in ether.

Incompatibility. Incompatibilities of sodium amidotrizoate with some antihistamines have been reported.

Adverse Effects and Treatment

Amidotrizoates and other iodinated contrast media may cause adverse effects due to direct toxicity, which tends to be dose-related and predictable, but use often leads to unpredictable or anaphylactoid reactions. Most reactions occur within 5 to 10 minutes and are mild and transient; however, severe, life-threatening reactions may also occur, and delayed reactions have been reported.

Direct toxic effects of iodinated contrast media are related to the osmolality of the solutions used and are most common with the amidotrizoates and other ionic monomeric compounds, which have a high osmolality. The route, the speed with which it is given, and the volume, concentration, and viscosity of the solution, also affect the incidence of adverse effects. For ionic media, the cation is also important: meglumine salts are generally better tolerated, but sodium salts have a lower viscosity and may produce fewer arrhythmias, and preparations containing a mixture of the salts are therefore often used. Anaphylactoid reactions are also more common with high-osmolality, ionic contrast media.