liver, and excreted in the urine. Less than 12% of a dose of thiamazole may be excreted as unchanged drug. 3-Methyl-2-thiohydantoin has been identified as a metabolite of thiamazole. The elimination half-life may be increased in hepatic and renal impairment.

Thiamazole crosses the placenta and is distributed into breast milk.

◊ References to the pharmacokinetics of carbimazole and thiamazole.

1. Skellern GG, *et al.* The pharmacokinetics of methimazole after oral administration of carbimazole and methimazole, in hyperthyroid patients. *Br J Clin Pharmacol* 1980; **9:** 137–43.
2. Kampmann JP, Hansen JM. Clinical pharmacokinetics of antithyroid drugs. *Clin Pharmacokinet* 1981; **6:** 401–28.
3. Jansson R, *et al.* Intrathyroidal concentrations of methimazole in patients with Graves' disease. *J Clin Endocrinol Metab* 1983; **57:** 129–32.
4. Cooper DS, *et al.* Methimazole pharmacology in man: studies using a newly developed radioimmunoassay for methimazole. *J Clin Endocrinol Metab* 1984; **58:** 473–9.
5. Jansson R, *et al.* Pharmacokinetic properties and bioavailability of methimazole. *Clin Pharmacokinet* 1985; **10:** 443–50.

Uses and Administration

Carbimazole is a thiourea antithyroid drug that acts by blocking the production of thyroid hormones (see p.2165). It is used in the management of hyperthyroidism (p.2165), including the treatment of Graves' disease, the preparation of hyperthyroid patients for thyroidectomy, as an adjunct to radio-iodine therapy, and in the treatment of thyroid storm.

Carbimazole is completely metabolised to thiamazole and it is this metabolite that is responsible for the antithyroid activity of carbimazole.

Carbimazole is given orally in a typical initial dosage of 15 to 40 mg daily, in divided doses; occasionally up to 60 mg daily may be required. Control of symptoms is usually achieved in 1 to 2 months. When the patient is euthyroid the dose is gradually reduced to the smallest amount that will maintain the euthyroid state. Typical maintenance doses are 5 to 15 mg daily, which may be given as a single daily dose.

Treatment in children should be undertaken by a specialist. The *BNFC* recommends an initial dose of 250 micrograms/kg three times daily for neonates and children up to 12 years of age. Children aged 12 to 18 years may be given 10 mg three times daily initially. Doses are adjusted according to response; higher initial doses may be needed in thyrotoxic crisis.

Carbimazole is also given orally in a dose of 20 to 60 mg daily, with supplemental levothyroxine, as a *blocking-replacement regimen*.

Either form of maintenance treatment is usually continued for at least a year, and often for 18 months; up to 2 years of treatment may be required.

Preparations

BP 2008: Carbimazole Tablets.

Proprietary Preparations (details are given in Part 3)
Austral.: Neo-Mercazole; ***Austria:*** Carbistad; ***Denm.:*** Neo-Mercazole; ***Fin.:*** Tyrazol; ***Fr.:*** Neo-Mercazole; ***Ger.:*** Car; Neo-Thyreostat†; ***Gr.:*** Thyrostat; ***Hong Kong:*** Cazole; ***India:*** Neo-Mercazole; ***Indon.:*** Neo-Mercazole; ***Irl.:*** Neo-Mercazole; ***Malaysia:*** Camazol†; ***Norw.:*** Neo-Mercazole; ***NZ:*** Neo-Mercazole; ***Philipp.:*** Neo-Mercazole; ***S.Afr.:*** Neo-Mercazole; ***Singapore:*** Camazol; Cazole†; ***Spain:*** Neo Tomizol; ***Switz.:*** Neo-Mercazole; ***UK:*** Neo-Mercazole.

Dibromotyrosine

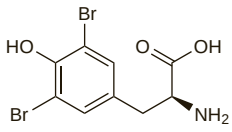
Dibromotirosina. 3,5-Dibromo-L-tyrosine.

$C_9H_9Br_2NO_3$ = 339.0.

CAS — 300-38-9.

ATC — H03BX02.

ATC Vet — QH03BX02.



Profile

Dibromotyrosine is an antithyroid drug used in the treatment of hyperthyroidism (p.2165) in doses of 300 to 900 mg daily by mouth.

Preparations

Proprietary Preparations (details are given in Part 3)
Ital.: Bromotiren.

Multi-ingredient: ***Ital.:*** Bromazolo.

Iodine

Iod; Iode; Iodium; Iodo; Iodum; Iyot; Jód; Jod; Jodas; Jodi; Jodum; Yodo.

I_2 = 253.80894.

CAS — 7553-56-2.

ATC — D08AG03.

ATC Vet — QD08AG03.

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

Ph. Eur. 6.2 (Iodine). Greyish-violet, brittle plates or fine crystals, with a metallic sheen. It is slowly volatile at room temperature. Very slightly soluble in water; soluble in alcohol; slightly soluble in glycerol; very soluble in concentrated solutions of iodides.

USP 31 (Iodine). Heavy, greyish-black plates or granules with a metallic sheen and a characteristic odour. Soluble 1 in 3000 of water, 1 in 13 of alcohol, 1 in 4 of carbon disulfide, and 1 in 80 of glycerol; freely soluble in chloroform, in ether, and in carbon tetrachloride; soluble in solutions of iodides. Store in airtight containers.

Incompatibility. With acetone, iodine forms a pungent irritating compound.

Potassium Iodate

Iodato potásico; Potasu jodan.

KIO_3 = 214.0.

CAS — 7758-05-6.

Pharmacopoeias. In *Br.*, *Chin.*, and *It.*

BP 2008 (Potassium Iodate). A white crystalline powder with a slight odour. Slowly soluble in water; insoluble in alcohol. A 5% solution in water has a pH of 5.0 to 8.0.

Potassium Iodide

Iodeto de Potássio; Ioduro potásico; Jodid draselný; Kalii Iodetum; Kalii iodidum; Kalii Jodidum; Kalio jodidas; Kalium Iodatum; Kalium Jodatum; Kaliumjodid; Kálium-jodid; Kaliumjodidi; Pot. Iod.; Potassii Iodidum; Potassium (Iodure de); Potassium, iodure de; Potasu jodek; Potasyum Iyodür.

KI = 166.0.

CAS — 7681-11-0.

ATC — R05CA02; S01XA04; V03AB21.

ATC Vet — QR05CA02; QS01XA04; QV03AB21.

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

Ph. Eur. 6.2 (Potassium Iodide). A white or almost white powder or colourless crystals. Very soluble in water; soluble in alcohol; freely soluble in glycerol. Protect from light.

USP 31 (Potassium Iodide). Hexahedral crystals, either transparent and colourless or somewhat opaque and white, or a white, granular powder. It is slightly hygroscopic. Soluble 1 in 0.7 of water and 1 in 0.5 of boiling water, 1 in 22 of alcohol, and 1 in 2 of glycerol. Its solutions are neutral or alkaline to litmus.

Sodium Iodide

Iodeto de Sódio; Ioduro sódico; Jodid sodný; Natrii Iodetum; Natrii iodidum; Natrii Jodidum; Natrio jodidas; Natrium Iodatum; Natriumjodid; Nátrium-jodid; Natriumjodidi; Sod. Iod.; Sodii Iodidum; Sodium (Iodure de); Sodium, iodure de; Sodu jodek; Sodyum Iyodür.

NaI = 149.9.

CAS — 7681-82-5.

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

Ph. Eur. 6.2 (Sodium Iodide). Colourless crystals or white or almost white, crystalline powder. It is hygroscopic. Very soluble in water; freely soluble in alcohol. Protect from light.

USP 31 (Sodium Iodide). Colourless, odourless crystals, or white crystalline powder. It is deliquescent in moist air and develops a brown tint upon decomposition. Soluble 1 in 0.6 of water, 1 in 2 of alcohol, and 1 in 1 of glycerol. Store in airtight containers.

Adverse Effects and Treatment

Iodine and iodides, whether applied topically or given systemically, can give rise to hypersensitivity reactions which may include urticaria, angioedema, cutaneous haemorrhage or purpuras, fever, arthralgia, lymphadenopathy, and eosinophilia.

Inhalation of iodine vapour is very irritating to mucous membranes.

Iodine and iodides have variable effects on the thyroid (see below) and can produce goitre and hypothyroidism as well as hyperthyroidism (the Iod-Basedow or Jod-Basedow phenomenon). Goitre and hypothyroidism have also occurred in infants born to mothers who had taken iodides during pregnancy.

Prolonged use may lead to a range of adverse effects, often called 'iodism', some of which may again be due to hypersensitivity. Adverse effects include metallic taste, increased salivation, burning or painful mouth; there may be acute rhinitis, coryza-like symptoms, and swelling and inflammation of the throat. Eyes may be irritated and swollen and there may be increased lachrymation. Pulmonary oedema, dyspnoea, and bronchitis may develop. Skin reactions include acneform or, more rarely, severe eruptions (iododerma). Other reported effects include depression, insomnia, impotence, headache, and gastrointestinal disturbances, notably nausea, vomiting, and diarrhoea.

The symptoms of acute poisoning from ingestion of iodine are mainly due to its corrosive effects on the gastrointestinal tract; a disagreeable metallic taste, vomiting, abdominal pain, and bloody diarrhoea occur. Thirst and headache have been reported. Systemic toxicity may lead to shock, tachycardia, hypotension, fever, metabolic acidosis and renal impairment. Death may be due to circulatory failure, oedema of the epiglottis resulting in asphyxia, aspiration pneumonia, or pulmonary oedema. Oesophageal stricture may occur if the patient survives the acute stage.

Victims of acute poisoning have been given copious draughts of milk or starch mucilage; lavage should probably not be attempted, and certainly not unless the ingested iodine was in sufficiently dilute form not to produce gastrointestinal corrosion. Other possible oral treatments include activated charcoal or sodium thiosulfate solution (usually as a 1% solution) to reduce iodine to the less toxic iodides.

Effects on the thyroid. Iodide may be isolated by the body from a variety of sources, including an iodine-rich diet, or some disinfectants and drugs containing iodine (see also under Amiodarone, p.1212). Although iodine is required for the production of thyroid hormones, excessive quantities can cause hyperthyroidism, or even paradoxical goitre and hypothyroidism.

The normal daily requirement ranges from 100 to 300 micrograms.[1,2] Quantities of 500 micrograms to 1 mg daily probably have no untoward effects on thyroid function in most cases.[2] When progressively larger doses are given there is an initial rise in thyroid hormone production, but at still higher doses, production decreases (the Wolff-Chaikoff effect). This effect is usually seen with doses of more than about 2 mg daily, but is normally transient, adaptation occurring on repeated dosage. In certain individuals a lack of adaptation produces a chronic inhibition of thyroid hormone synthesis leading to goitre and **hypothyroidism**.[1,2]

Excess iodine may also induce **hyperthyroidism** (the Iod-Basedow or Jod-Basedow phenomenon). Iodine-induced hyperthyroidism has been associated with iodine prophylaxis programmes in developing countries.[3] The highest incidence of hyperthyroidism has been reported to occur 1 to 3 years after supplementation begins, with the incidence returning to normal within 3 to 10 years despite continued iodine exposure.[4] Elderly subjects and those with nodular goitres have been found to be at greatest risk.

To overcome any adverse effects on thyroid function as a result of iodine prophylaxis during **pregnancy**, WHO has issued guidelines on the safe use of iodised oil during gestation.[5,6] There is some evidence that the use of iodine-containing antiseptics on pregnant women and neonates may cause disturbances in thyroid function.[7,8]

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8. Weber G *et al.* Neonatal transient hypothyroidism: aetiological study. *Arch Dis Child Fetal Neonatal Ed* 1998; **79:** F70–2.