Methylmethacrylate monomer acts as a peripheral vasodilator and has caused hypotension and, rarely, cardiac arrest and death when absorbed during the use of polymethylmethacrylate (PMMA) as a bone cement during orthopaedic surgery. Other adverse effects associated with the use of polymethylmethacrylate as a bone cement include thrombophlebitis, pulmonary embolism, haemorrhage, haematoma, short-term irregularities in cardiac conduction, cerebrovascular accident, compression of the spinal cord and/or nerve roots, and new fractures in adjacent non-augmented vertebrae. Recommendations when using PMMA include monitoring with high quality imaging systems to detect leakage, and close monitoring of blood pressure during and immediately after the procedure.

**Effects on the nervous system.** Sensory polyneuropathy has been reported in a dental technician after occupational exposure to methylmethacrylate monomer.[1]

1. Sadoh DR, *et al.* Occupational exposure to methyl methacrylate monomer induces generalised neuropathy in a dental technician. *Br Dent J* 1999; **186:** 380–1.

## Uses and Administration

Methylmethacrylate forms the basis of acrylic bone cements used in orthopaedic surgery. A liquid consisting chiefly of methylmethacrylate monomer with a polymerisation initiator is mixed with a powder consisting of polymethylmethacrylate (PMMA) or a methylmethacrylate ester copolymer. The reaction is exothermic. Barium sulfate or zirconium dioxide may be added as a contrast medium. Polymethylmethacrylate beads containing gentamicin have been implanted for the prophylaxis and treatment of bone infections and some soft-tissue infections. Bone cements containing antibacterials such as gentamicin or erythromycin are also available.

Polymethylmethacrylate has also been used as a material for intra-ocular lenses, for denture bases, as a cement for dental prostheses, and in composite resins for dental restoration.

A number of polymers based on methacrylic acid are used in pharmaceutical technology mainly as film coating agents and binders.

Ph. Eur. 6.2 includes:

- Ammonio Methacrylate Copolymer (Type A) (a copolymer of acrylic and methacrylic acid esters)
- Ammonio Methacrylate Copolymer (Type B) (a copolymer of acrylic and methacrylic acid esters)
- Basic Butylated Methacrylate Copolymer
- Methacrylic Acid-Methyl Methacrylate Copolymer (1:1)
- Methacrylic Acid-Ethyl Acrylate Copolymer (1:1)
- Methacrylic Acid-Ethyl Acrylate Copolymer (1:1) Dispersion 30 per cent
- Methacrylic Acid-Methyl Methacrylate Copolymer (1:2)
- Polyacrylate Dispersion 30 per cent (a dispersion of an ethyl-acrylate-methyl methacrylate copolymer in water)

USNF 26 includes:

- Methacrylic Acid Copolymer (a copolymer of methacrylic acid and an acrylic or methacrylic ester)
- Amino Methacrylate Copolymer
- Ammonio Methacrylate Copolymer
- Ammonio Methacrylate Copolymer Dispersion
- Ethyl Acrylate and Methyl Methacrylate Copolymer

**Bone disorders.** Polymethylmethacrylate bone cements may be injected percutaneously into vertebral fractures or lesions to relieve pain and stabilise the damaged vertebra.[1-6] The technique has been used in the treatment of metastatic bone lesions and myeloma (p.660 and p.658) as well as for vertebral compression fractures due to osteoporosis (p.1084). Complications[5,7-9] are uncommon but may include both local and systemic effects (including pulmonary embolism) due to leakage of the cement and sudden drop in blood pressure, probably due to the monomer.

1. Barr JD, *et al.* Percutaneous vertebroplasty for pain relief and spinal stabilization. *Spine* 2000; **25:** 923–8.
2. Lingar L. Percutaneous polymethacrylate vertebroplasty. *Radiol Technol* 2004; **76:** 109–13.
3. Burton AW, *et al.* Vertebroplasty and kyphoplasty: a comprehensive review. *Neurosurg Focus* 2005; **18:** e1. Available at: http://www.medscape.com/viewarticle/501670 (accessed 15/02/06)
4. Suresh SP, Whitehouse RW. Vertebroplasty and kyphoplasty. *J Br Menopause Soc* 2005; **11:** 28–32.
5. Guglielmi G, *et al.* Percutaneous vertebroplasty: indications, contraindications, technique, and complications. *Acta Radiol* 2005; **46:** 256–68.
6. Hochmuth K, *et al.* Percutaneous vertebroplasty in the therapy of osteoporotic vertebral compression fractures: a critical review. *Eur Radiol* 2006; **16:** 998–1004.
7. Laredo JD, Hamze B. Complications of percutaneous vertebroplasty and their prevention. *Semin Ultrasound CT MR* 2005; **26:** 65–80.
8. Barragan-Campos HM, *et al.* Percutaneous vertebroplasty for spinal metastases: complications. *Radiology* 2006; **238:** 354–62.
9. Health Canada. Complications associated with the use of bone cements in vertebroplasty and kyphoplasty procedures (issued 30th May, 2007). Available at: http://www.hc-sc.gc.ca/ dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/bone_cement-ciment_acrylique_nth-aah_2_e.pdf (accessed 30/5/08)

## Preparations

**Proprietary Preparations** (details are given in Part 3)
***Chile:*** Palacos E†; Palacos R; ***Ger.:*** CMW; flint; Palacos R; Palamed; SmartSet HV; ***Port.:*** Septopal; ***Singapore:*** Palacos R†; ***Thai.:*** Palacos R; ***UK:*** Palacos R.

**Multi-ingredient:** ***Arg.:*** Septopal†; ***Austral.:*** Palacos E with Garamycin; Palacos R with Garamycin; Septopal; ***Austria:*** Septopal; ***Belg.:*** Palacos LV avec Gentamicine†; Palacos R avec Gentamicine†; Septopal; ***Braz.:*** Septopal; ***Chile:*** Palacos E con Gentamicina; Palacos R con Gentamicina; Perlas De PMMA con Gentamicina; ***Cz.:*** Septopal†; ***Denm.:*** Septopal; ***Fin.:*** Palacos R cum Gentamicin†; Septopal; ***Fr.:*** Palacos LV avec Gentamicine; Palacos R avec Gentamicine; ***Ger.:*** CMW mit Gentamicin; Copal; Epiglu; Palamed G; Refobacin-Palacos R; Septopal; SmartSet GHV; ***Gr.:*** Palacos R with Gentamycin†; Septopal†; ***Hong Kong:*** Septopal; ***Hung.:*** Plastubol†; Septopal; ***India:*** Septopal; ***Irl.:*** Epiglu; ***Malaysia:*** Septopal†; ***Neth.:*** Septopal; ***Norw.:*** Septopal; ***NZ:*** Antibiotic Simplex; CMW Gentamicin; Palacos with Garamycin; Vacu-Mix Plus with CMW gentamicin; ***Philipp.:*** Septopal; ***S.Afr.:*** Palacos R with Garamycin; Septopal; ***Singapore:*** Refobacin Bone Cement R; Refobacin-Palacos R†; Septopal†; ***Swed.:*** Septopal†; ***Switz.:*** Septopal; ***Thai.:*** Refobacin-Palacos R; Septopal; ***UK:*** Epiglu; Palacos LV with Gentamicin; Palacos R with Gentamicin; Septopal.

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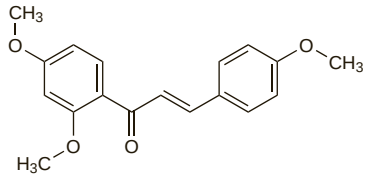
# Metochalcone *(rINN)*

CB-1314; Methochalcone; Metocalcona; Métochalcone; Metochalconum; Trimethoxychalcone. 2′,4,4′-Trimethoxychalcone.

Метохалкон

$C_{18}H_{18}O_4$ = 298.3.
*CAS — 18493-30-6.*



## Profile

Metochalcone has been used as a choleretic.

## Preparations

**Proprietary Preparations** (details are given in Part 3)
**Multi-ingredient:** ***Spain:*** Neocolan.

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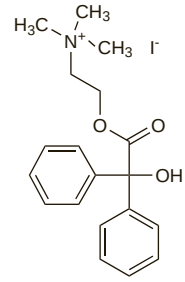
# Metocinium Iodide *(pINN)*

Ioduro de metocinio; Metocinii Iodidum; Métocinium, Iodure de. (2-Hydroxyethyl)trimethylammonium iodide benzilate.

Метоциния Йодид

$C_{19}H_{24}INO_3$ = 441.3.
*CAS — 2424-71-7.*



## Profile

Metocinium iodide is used as an antispasmodic.

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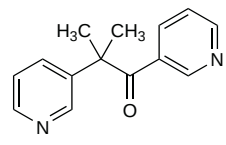
# Metyrapone *(BAN, USAN, rINN)*

Metirapon; Metirapona; Metyrapon; Métyrapone; Metyraponi; Metyraponum; Su-4885 (metyrapone tartrate). 2-Methyl-1,2-di(3-pyridyl)propan-1-one.

Метирапон

$C_{14}H_{14}N_2O$ = 226.3.
*CAS — 54-36-4.*
*ATC — V04CD01.*
*ATC Vet — QV04CD01.*



**Pharmacopoeias.** In *Br.*, *Jpn*, and *US*.
**BP 2008** (Metyrapone). A white to light amber crystalline powder with a characteristic odour. M.p. 50° to 53°. Sparingly soluble in water; freely soluble in alcohol and in chloroform; it dissolves in dilute mineral acids. Protect from light.
**USP 31** (Metyrapone). A white to light amber, fine, crystalline powder, having a characteristic odour. It darkens on exposure to light. Sparingly soluble in water; soluble in chloroform and in methyl alcohol; forms water-soluble salts with acids. Store in air-tight containers. Protect from heat and light.

## Adverse Effects

Metyrapone may give rise to nausea and vomiting, abdominal pain, headache, sedation, dizziness, hypotension, and hypersensitivity rashes. Hypoadrenalism, hirsutism, and bone marrow depression may occur rarely. Long-term use of metyrapone can cause hypertension.

**Alopecia.** Reports of alopecia[1,2] associated with administration of metyrapone for Cushing's syndrome.

1. Harris PL. Alopecia associated with long-term metyrapone use. *Clin Pharm* 1986; **5:** 66–8.
2. Harries-Jones R, Overstall P. Metyrapone-induced alopecia. *Postgrad Med J* 1990; **66:** 584.

## Precautions

Metyrapone should be used with extreme caution, if at all, in patients with gross hypopituitarism or with reduced adrenal secretory activity because of the risk of precipitating acute adrenal failure. Thyroid dysfunction or liver cirrhosis may alter the response to metyrapone.

Dizziness and sedation may affect the performance of skilled tasks such as driving.

**Porphyria.** Metyrapone is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *in-vitro* systems.

## Interactions

Phenytoin is reported to increase the metabolism of metyrapone; doubling the dose of metyrapone may counteract the interaction. However, as many other drugs may interfere with steroid assessment, medication is best avoided where possible during the metyrapone test. Drugs reported to interfere with the metyrapone test include antidepressants such as amitriptyline, antithyroid drugs, antipsychotics such as chlorpromazine, barbiturates, corticosteroids, cyproheptadine, and hormones that affect the hypothalamic-pituitary axis such as oestrogens and progestogens.

## Pharmacokinetics

Metyrapone is rapidly absorbed from the gastrointestinal tract. It is metabolised by rapid reduction to metyrapol and excreted in the urine as glucuronide conjugates of metyrapone and metyrapol.

## Uses and Administration

Metyrapone inhibits the enzyme 11β-hydroxylase responsible for the synthesis of the glucocorticoids cortisone and hydrocortisone (cortisol) as well as aldosterone from their precursors. The consequent fall in the plasma concentrations of circulating glucocorticoids stimulates the anterior pituitary gland to produce more corticotropin. This, in turn, stimulates the production of more 11-deoxycortisol and other precursors which are metabolised in the liver and excreted in the urine where they can be measured. Metyrapone is therefore used as a test of the feedback hypothalamic-pituitary mechanism in the diagnosis of Cushing's syndrome, although the dexamethasone suppression test (p.1527) may be preferred.

After demonstration of the responsiveness of the adrenal cortex, metyrapone is given orally, usually in a dose of 750 mg every 4 hours for 6 doses. Taking doses with milk or after a meal may minimise the gastrointestinal adverse effects of metyrapone. A suggested oral dose for children is 15 mg/kg, with a minimum dose of 250 mg, every 4 hours for 6 doses. In patients with a normally functioning pituitary gland excretion of 17-hydroxycorticosteroids is increased two- to fourfold and that of 17-ketosteroids about twofold.

Metyrapone is also used in the management of Cushing's syndrome (below) when doses may range from 250 mg to 6 g daily.

Since metyrapone inhibits the synthesis of aldosterone it has been used to treat some cases of resistant oedema; it is given with a glucocorticoid to suppress the normal corticotropin response to low plasma concentrations of glucocorticoids. The suggested usual dosage of metyrapone in resistant oedema is 3 g daily in divided doses.

Metyrapone tartrate has also been used.

**Cushing's syndrome.** Cushing's syndrome is the result of a chronic excess of glucocorticoids.[1,2] It may be independent of the secretion of adrenocorticotrophic hormone (ACTH; corticotropin), either due to an adrenal tumour secreting cortisol, or to exogenous corticosteroids, or it may be ACTH-dependent, such as Cushing's disease proper, which is caused by excessive ACTH secretion from a pituitary adenoma; other ACTH-dependent forms may be due to pituitary hyperplasia, or an ectopic ACTH-secreting tumour elsewhere—usually bronchus or lung cancer. About two-thirds of all cases are due to Cushing's disease, which is 8 times more common in women than men.

Symptoms may develop insidiously over several years and include obesity, particularly of the trunk, rounding of the face,

atrophy of the skin leading to striae, poor wound healing, muscle weakness, osteoporosis, hypertension, diabetes mellitus, and depression and other psychological disturbances. Hypokalaemia is rare in Cushing's disease but common in other forms of the syndrome. Women may have hirsutism due to adrenal androgen secretion, and both sexes may develop hypogonadism and loss of libido.

**Diagnosis** of Cushing's syndrome can be problematic because no test is wholly reliable.[1,3-6] Where there is suspicion, options for initial screening include measurement of urinary cortisol, late-night salivary cortisol, midnight plasma-cortisol, and overnight low-dose dexamethasone suppression testing. A dexamethasone-corticorelin test may be used to identify pseudo-Cushing's conditions such as depression or alcoholism. Once a diagnosis of Cushing's syndrome has been made, plasma-ACTH measurements are used to distinguish between ACTH-dependent and ACTH-independent forms. High-dose dexamethasone suppression testing and corticorelin stimulation testing have been used to differentiate between pituitary and ectopic ACTH-dependent Cushing's syndrome, but they both have disadvantages and their usefulness has been debated. For further discussion of dexamethasone suppression testing, see p.1527, and for corticorelin stimulation testing, see p.1523. Imaging techniques and sampling of central (petrosal) venous blood are additional procedures that may be used for localising tumours.

Appropriate **treatment** depends on accurate identification of the cause of the syndrome.[1] The usual treatment in Cushing's disease is transsphenoidal resection of the tumour, which when carried out by an experienced surgeon produces a successful response in the majority of patients. Pituitary radiotherapy is slower than surgery to take effect, produces a lower remission rate, and is more likely to produce hypopituitarism. It is therefore usually used as second-line therapy when initial surgery has not been curative and a second operation is considered unsuitable. If pituitary surgery or radiotherapy fails, bilateral adrenalectomy may be considered (although this has some risks including that of Nelson's syndrome due to hyperactivity of residual pituitary tumour). Patients who undergo such surgery require glucocorticoid and mineralocorticoid replacement therapy for life. Surgery is also the treatment of choice for a resectable adrenal tumour or ectopic ACTH-secreting tumour; even where there is metastasis it may be useful in moderating symptoms.

A number of drugs have been used in patients with Cushing's disease, but their role appears to be mainly adjuvant.[1,7] Drugs acting at the hypothalamic-pituitary level, aimed at reducing ACTH secretion, do not seem to be of much value; there have been occasional reports of benefit with bromocriptine, cyproheptadine, and sodium valproate. Drugs that inhibit steroid synthesis in the adrenal gland are more effective, and include mitotane, metyrapone, and ketoconazole. These may be used to control severe complications quickly, prepare patients for surgery, or provide cover while radiotherapy takes effect. Mifepristone acts as a glucocorticoid receptor antagonist, and has been used successfully in a few patients with Cushing's syndrome. Etomidate can be useful for acute control of hypercortisolaemia if the oral route is not available.

In patients with the ectopic ACTH syndrome in whom surgery is unsuitable or ineffective, chemotherapy aimed at the primary tumour is the treatment of choice but is likely to be only palliative. Inhibitors of steroid synthesis can be used to control symptoms, and somatostatin analogues such as octreotide may decrease ACTH secretion by ectopic tumours that have somatostatin receptors.[1]

Surgery is the preferred treatment for an adrenal tumour but, although this is usually curative for adrenal adenoma, it is less successful for adrenal carcinoma.[1]

In patients who are successfully treated for Cushing's syndrome adrenocortical replacement therapy (see p.1498) is usually required until the hypothalamic-pituitary-adrenal axis recovers normal function, a process which may take many months.


1. Newell-Price J, *et al.* Cushing's syndrome. *Lancet* 2006; **367:** 1605–17.
2. Newell-Price J, *et al.* Cushing's syndrome. *Lancet* 2006; **367:** 1605–17.
3. Raff H, Findling JW. A physiologic approach to diagnosis of the Cushing syndrome. *Ann Intern Med* 2003; **138:** 980–91.
4. Arnaldi G, *et al.* Diagnosis and complications of Cushing's syndrome: a consensus statement. *J Clin Endocrinol Metab* 2003; **88:** 5593–5602.
5. Findling JW, Raff H. Cushing's syndrome: important issues in diagnosis and management. *J Clin Endocrinol Metab* 2006; **91:** 3746–53.
6. Nieman LK, *et al.* The diagnosis of Cushing's syndrome: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2008; **93:** 1526–40. Also available at: http://www.endo-society.org/guidelines/final/upload/Cushings_Guideline.pdf (accessed 06/08/08)
7. Nieman LK. Medical therapy of Cushing's disease. *Pituitary* 2002; **5:** 77–82.


### Preparations

***BP 2008:*** Metyrapone Capsules;
***USP 31:*** Metyrapone Tablets.

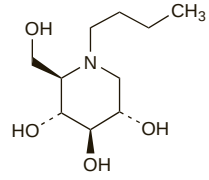
**Proprietary Preparations** (details are given in Part 3)
***Austral.:*** Metopirone; ***Cz.:*** Metopirone†; ***Fr.:*** Metopirone; ***Gr.:*** Metopirone; ***Irl.:*** Metopirone; ***Israel:*** Metopirone; ***Neth.:*** Metopiron; ***NZ:*** Metopirone; ***Swed.:*** Metopiron; ***Switz.:*** Metopirone; ***UK:*** Metopirone; ***USA:*** Metopirone.

## Miglustat *(BAN, USAN, rINN)*

Butyldeoxynojirimycin; *n*-Butyl-deoxynojirimycin; Miglustaatti; Miglustatum; OGT-918; OXAIDS; SC-48334. 1,5-(Butylimino)-1,5-dideoxy-D-glucitol; (2*R*,3*R*,4*R*,5*S*)-1-Butyl-2-(hydroxymethyl)piperidine-3,4,5-triol.

Миглустат

$C_{10}H_{21}NO_4$ = 219.3.
*CAS — 72599-27-0.*
*ATC — A16AX06.*
*ATC Vet — QA16AX06.*




### Adverse Effects and Precautions

Diarrhoea and other gastrointestinal disturbances, weight loss, tremor, dizziness, headache, cramps, and visual disturbances are frequent in patients receiving miglustat, and some patients may experience paraesthesias, peripheral neuropathy, or thrombocytopenia. Studies in *animals* have indicated an effect on spermatogenesis; male patients should not attempt conception during, or for 3 months after stopping, treatment. Care is required in renal impairment.

### Pharmacokinetics

Miglustat is rapidly absorbed after oral doses with maximum plasma concentrations reached in about 2 hours. It is mainly excreted in the urine with some also excreted in the faeces; the average elimination half-life is 6 to 7 hours.

**Food.** The average peak plasma concentration was reduced by 37% when miglustat was taken with food by 24 healthy subjects. However, there was no clinically significant effect on the extent of absorption (area under the curve was decreased by 14%).[1] Licensed product information states that miglustat may be taken with or without food.


1. van Giersbergen PLM, Dingemanse J. Influence of food intake on the pharmacokinetics of miglustat, an inhibitor of glucosylceramide synthase. *J Clin Pharmacol* 2007; **47:** 1277–82.


### Uses and Administration

Miglustat is an inhibitor of the enzyme glucosylceramide synthase, responsible for the first step in the synthesis of glucosylceramide and most other glycolipids. It is used to help prevent the accumulation of glucosylceramide in patients with mild to moderate type 1 Gaucher disease (p.2249) who cannot be treated with enzyme replacement therapy. The initial dose is 100 mg orally 3 times daily; reduction to 100 mg once or twice daily may be necessary in some patients because of diarrhoea. For details of reduced doses in patients with renal impairment, see below. Miglustat has also been used for the treatment of Niemann-Pick disease, type C.

◊ References.


1. McCormack PL, Goa KL. Miglustat. *Drugs* 2003; **63:** 2427–34.
2. Weinreb NJ, *et al.* Guidance on the use of miglustat for treating patients with type 1 Gaucher disease. *Am J Hematol* 2005; **80:** 223–9.
3. Giraldo P, *et al.* Short-term effect of miglustat in every day clinical use in treatment-naïve or previously treated patients with type 1 Gaucher's disease. *Haematologica* 2006; **91:** 703–6.
4. Elstein D, *et al.* Oral maintenance clinical trial with miglustat for type I Gaucher disease: switch from or combination with intravenous enzyme replacement. *Blood* 2007; **110:** 2296–2301.
5. Patterson MC, *et al.* Miglustat for treatment of Niemann-Pick C disease: a randomised controlled study. *Lancet Neurol* 2007; **6:** 765–72.


**Administration in renal impairment.** The initial dose of miglustat should be reduced in renal impairment according to the patient's creatinine clearance (CC):

- CC 50 to 70 mL/minute per 1.73 $m^2$: 100 mg twice daily
- CC 30 to 50 mL/minute per 1.73 $m^2$: 100 mg daily
- CC less than 30 mL/minute per 1.73 $m^2$: not recommended

### Preparations

**Proprietary Preparations** (details are given in Part 3)
***Belg.:*** Zavesca; ***Canad.:*** Zavesca; ***Cz.:*** Zavesca; ***Denm.:*** Zavesca; ***Fin.:*** Zavesca; ***Fr.:*** Zavesca; ***Ger.:*** Zavesca; ***Gr.:*** Zavesca; ***Hung.:*** Zavesca; ***Israel:*** Zavesca; ***Ital.:*** Zavesca; ***Neth.:*** Zavesca; ***Norw.:*** Zavesca; ***Port.:*** Zavesca; ***Spain:*** Zavesca; ***Swed.:*** Zavesca; ***Switz.:*** Zavesca; ***UK:*** Zavesca; ***USA:*** Zavesca.

## Dementholised Mint Oil

Csökkentett mentoltartalmú mezei mentaolaj (partly dementholised mint oil); Menta, aceite esencial desmentolado de; Mentha arvensis, huile essentielle partiellement démentholée de (mint oil, partly dementholised); Menthae arvensis aetheroleum partim mentholum depletum (mint oil, partly dementholised).
*CAS — 68917-18-0 (cornmint oil).*

**Pharmacopoeias.** In *Eur.* (see p.vii).
Mentha oil is in *Jpn.*
**Ph. Eur. 6.2** (Mint Oil, Partly Dementholised; Menthae Arvensis Aetheroleum Partim Mentholum Depletum; Dementholised Mint Oil BP 2008). The essential oil obtained by steam distillation from the fresh, flowering aerial parts, recently gathered from *Mentha canadensis* (*M. arvensis* var. *glabrata*; *M. arvensis* var. *piperascens*) followed by partial separation of menthol by crystallisation. A colourless or pale yellow to greenish-yellow liquid with a characteristic odour. Store in well-filled airtight containers at a temperature not exceeding 25°. Protect from light.

### Profile

Dementholised mint oil is used as a flavour. *Mentha arvensis* is used in herbal medicine as a febrifuge and for rheumatic disorders. Cornmint oil, obtained from *M. arvensis*, is used in aromatherapy as an adulterant or substitute for peppermint oil. Peppermint oil (p.1761) and spearmint oil (p.2391) are used as carminatives and flavours.

### Preparations

**Proprietary Preparations** (details are given in Part 3)
***Ger.:*** Japanol; JHP Rodler; Retterspitz Muskel- und Nervenol; ***Pol.:*** Migrenol; ***Switz.:*** Carmol; Minthi JHP Huile.

**Multi-ingredient:** ***Austral.:*** Tiger Balm White; ***Austria:*** Parodontax; ***Chile:*** Astrijesan; Calmatol; ***Ger.:*** Dreierlei; Trachiform†; ***Israel:*** Tiger Balm Red; Tiger Balm White; ***Ital.:*** Broncosedina; Listerine Fresh Citrus; Listerine Tartar Control; Venalta; ***Malaysia:*** Eucarbon†; ***Pol.:*** Argol Essenza Balsamica; Milocardin; Mucosit; Rapacholin C; Rapacholin Forte; Rhin-Bac; Salviasept; ***Switz.:*** GU Eau†; Huile analgesique "Temple of Heaven" contre les maux de tete†; Malveol; Neo-Angin au miel et citron; Neo-Angin sans sucre; Novital; Odontal; Onguent nasal Ruedi; Osa gel dentaire aux plantes; Parodontax F†; Parodontax†; Pastilles pectorales Demo N; Pommade nasale de Nager; Pommade nasale de Ruedi; Pommade Nasale Radix†; Radix; Tyrothricin; Unathene; Unatol; ***Turk.:*** Sandolin; ***UK:*** Olbas; Olbas for Children; Sinose.

## Miracle Fruit

Fruta milagrosa.

### Profile

Miracle fruit is the fruit of *Synsepalum dulcificum* (*Richardella dulcifica*) (Sapotaceae). It contains a glycoprotein 'miraculin' with no apparent taste of its own but which is able to make sour substances taste sweet and to improve the flavour of foods. Its activity is reduced by heating.

## Mistletoe

European Mistletoe; Gui; Mistelkraut; Muérdago; Tallo de Muérdago; Visci Caulis; Visci herba; Viscum; Viscum Album.

**Pharmacopoeias.** In *Ger.*

### Profile

Mistletoe is the dried, evergreen, dioecious semi-parasite, *Viscum album* (Loranthaceae), which grows on the branches of deciduous trees, chiefly apple, poplar, and plum. It occurs as a mixture of broken stems and leaves and occasional fruits. Mistletoe has a vasodilator action and has been used in herbal preparations for hypertension and cardiovascular disorders although its activity when taken orally is questionable. It has also been used in nervous disorders.

Mistletoe contains lectins with cytotoxic and immunomodulatory actions *in vitro* and preparations have been given by injection in a number of neoplastic diseases.

Ingestion of the berries and other parts has been reported to cause nausea, vomiting, diarrhoea, and bradycardia.

**Homoeopathy.** Mistletoe has been used in homoeopathic medicines under the following names: Viscum album; Vis. alb.

◊ A review of mistletoe.[1] There are about 1300 species of mistletoe representing 36 genera of the Loranthaceae, and what is called the "common mistletoe" varies from country to country: in Europe the term describes *Viscum album* while in the USA it describes *Phoradendron flavescens*. The toxicity of aqueous extracts of mistletoe has been found to depend upon the nature of the host plant. Three classes of cytotoxic compounds are present in the leaves and stems of *V. album* although the berries are generally considered to be the most toxic part of the plant. These are alkaloids, viscotoxins, and lectins. The viscotoxins have been shown to cause hypotension, bradycardia, arterial vasoconstriction, and a negative inotropic effect, and may act as acetylcholine agonists. The lectins show toxic effects in *animals* similar to those seen with ricin.


1. Anderson LA, Phillipson JD. Mistletoe—the magic herb. *Pharm J* 1982; **229:** 437–9.


**Adverse effects.** There have been reports of hepatitis after the ingestion of herbal remedies containing mistletoe.[1,2] Severe delayed hypersensitivity has been reported[3] in a patient given intravenous chemotherapy for breast cancer concurrently with subcutaneous injections of a mistletoe extract. It was thought that mistletoe had stimulated the reaction to methotrexate and gemcitabine.


1. Harvey J, Colin-Jones DG. Mistletoe hepatitis. *BMJ* 1981; **282:** 186–7.