5. Kvale PA, *et al.* American College of Chest Physicians. Lung cancer: palliative care. *Chest* 2003; **123** (suppl): 284S–311S. Also available at: http://www.chestjournal.org/cgi/reprint/123/1_suppl/284S.pdf (accessed 26/06/08)
6. Qaseem A, *et al.* Clinical Efficacy Assessment Subcommittee of the American College of Physicians. Evidence-based interventions to improve the palliative care of pain, dyspnea, and depression at the end of life: a clinical practice guideline from the American College of Physicians. *Ann Intern Med* 2008; **148:** 141–6. Also available at: http://www.annals.org/cgi/reprint/148/2/141.pdf (accessed 28/08/08)
7. Lorenz KA, *et al.* Evidence for improving palliative care at the end of life: a systematic review. *Ann Intern Med* 2008; **148:** 147–59.
8. Chandler S. Nebulized opioids to treat dyspnea. *Am J Hosp Palliat Care* 1999; **16:** 418–22.
9. Foral PA, *et al.* Nebulized opioids use in COPD. *Chest* 2004; **125:** 691–4.
10. Brown SJ, *et al.* Nebulized morphine for relief of dyspnea due to chronic lung disease. *Ann Pharmacother* 2005; **39:** 1088–92.
11. Kallet RH. The role of inhaled opioids and furosemide for the treatment of dyspnea. *Respir Care* 2007; **52:** 900–10.

Pain. Opioid analgesics are used for the relief of acute and chronic pain (see Choice of Analgesic, p.2). Not every type of pain responds; neuropathic pain, for example, may not be alleviated by opioid therapy. For further discussion of specific pain states and the role of opioid analgesics in their treatment see p.5 onwards.

There has also been interest in the local analgesic effects of opioids themselves.[1,2]

The use of opioid analgesics in opioid-dependent patients receiving maintenance treatment with an opioid is the subject of much debate; however, some consider such use to be appropriate in the management of acute pain in these patients and recommendations have been issued.[3]

1. Thompson DF, Pierce DR. Local analgesia with opioid drugs. *Ann Pharmacother* 1995; **29:** 189–90.
2. Stein C. The control of pain in peripheral tissue by opioids. *N Engl J Med* 1995; **332:** 1685–90.
3. Alford DP, *et al.* Acute pain management for patients receiving maintenance methadone or buprenorphine therapy. *Ann Intern Med* 2006; **144:** 127–34.

HEADACHE. Opioid analgesics such as codeine are sometimes included in oral compound analgesic preparations used in the initial treatment of migraine (see p.616) or tension-type headache (see p.617), but are best avoided, especially in patients who experience frequent attacks.

Restless legs syndrome. Some opioids may be beneficial in the treatment of restless legs syndrome (see Sleep-associated Movement Disorders, p.958), although evidence is scanty.

Sedation. In addition to their analgesic action opioids have been used for their sedative properties. Mention of this use of opioids can be found in the discussions of anaesthesia (p.1780), endoscopy (p.956), and intensive care (p.957).

Tetanus. Opioid analgesics can be used to provide analgesia and additional sedation in patients undergoing treatment for tetanus (p.196 and p.1901). Opioids such as fentanyl, morphine, and sufentanil have also been given to control the sympathetic overactivity in such patients.[1-3]

1. Rocke DA, *et al.* Morphine in tetanus—the management of sympathetic nervous system overactivity. *S Afr Med J* 1986; **70:** 666–8.
2. Moughabghab AV, *et al.* Management of autonomic dysfunction in severe tetanus: the use of fentanyl. *Can J Anaesth* 1995; **42:** 955.
3. Bhagwanjee S, *et al.* Management of sympathetic overactivity in tetanus with epidural bupivacaine and sufentanil: experience with 11 patients. *Crit Care Med* 1999; **27:** 1721–5.

Opium

Gum Opium; Nyers ópium; Opijus, žaliavinis; Opio; Opium brut; Opium crudum; Opium surové; Raakaopiumi; Råopium; Raw Opium.

Опиум

ATC — A07DA02; N02AA02.
ATC Vet — QA07DA02; QN02AA02.

NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of opium:
Ah-pen-yen; Aunti; Aunti Emma; Big O; Black; Black pill; Black shit; Black stuff; Black tar opium; Block; Boulette; Chandoo; Chandu; China; Chinese molasses; Chinese tobacco; Chocolate; Cruz; Dopium; Dover's deck; Dover's powder; Dream gum; Dream gun; Dream stick; Dreams; Dutch courage; Easing powder; Fi-do-nie; Gee; God's medicine; Goma; Gondola; Gong; Goric; Great tobacco; Gum; Guma; Hard stuff; Hocus; Hop; Hops; Incense; Indonesian bud; Joy plant; Midnight oil; Mira; Mud; O; O.P.; Ope; O-Rock DC; Pen yan; Pin gon; Pin yen; Pox; Skee; Tar; Toxy; Toys; When-shee; Ze; Zero.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *US*.
Chin., *Eur.*, and *US* include a monograph for prepared or powdered opium. *Eur.* also contains monographs for standardised opium dry extract or standardised opium tincture. *Jpn* includes prepared opium and a diluted opium powder containing 1% of anhydrous morphine.
Ph. Eur. 6.2 (Opium, Raw; Opium BP 2008). The air-dried latex obtained by incision from the unripe capsules of *Papaver somniferum* L. It has a characteristic odour and a blackish-brown colour. It should contain not less than 10% of anhydrous morphine, not less than 2% of anhydrous codeine, and not more than 3% of anhydrous thebaine. Protect from light.
Ph. Eur. 6.2 (Opium, Prepared; Opii Pulvis Normatus). Raw opium powdered and dried at a temperature not exceeding 70°. It is a yellowish-brown or dark brown powder and contains 9.8 to 10.2% of morphine and not less than 1.0% of codeine, calculated with reference to the dried drug. The content may be adjusted by adding a suitable excipient or raw opium powder.
USP 31 (Opium). The air-dried milky exudate obtained by incising the unripe capsules of *Papaver somniferum* (Papaveraceae). Externally it is pale olive-brown or olive-grey; internally it is reddish-brown. It has a very characteristic odour and a very bitter taste. It yields not less than 9.5% of anhydrous morphine.
USP 31 (Powdered Opium). Opium dried at a temperature not exceeding 70°, and reduced to a very fine light brown or moderately yellowish-brown powder that yields not less than 10% and not more than 10.5% of anhydrous morphine. It may contain any of the permitted diluents with the exception of starch.

Profile

Opium is the air-dried latex obtained by incision from the unripe capsules of *Papaver somniferum* (Papaveraceae). It contains morphine, codeine, and thebaine and a variable mixture of other alkaloids including noscapine and papaverine. The exuded latex is dried and manipulated to form cakes of uniform composition, variously shaped according to the country of origin, and known in commerce as Turkish, Indian, or European opium.

Opium has the properties of opioid analgesics (p.101). Its analgesic and sedative actions are due mainly to its content of morphine (p.89). It acts less rapidly than morphine since opium appears to be more slowly absorbed; the relaxing action of the papaverine and noscapine on intestinal muscle makes it more constipating than morphine.

Opium is intended only as the starting material for the manufacture of galenical preparations and is not dispensed as such. It is used as Prepared Opium (Ph. Eur. 6.2), as Powdered Opium (USP 31), as Opium Tincture (BP 2008 or USP 31), or as Camphorated Opium Tincture (BP 2008) or Paregoric (USP 31) in various oral preparations. These have included Opiate Squill Linctus (BP 2008) (Gee's linctus) for cough.

Paregoric (USP 31) has been advocated in the USA for the treatment of neonatal abstinence syndrome.

Abuse. Reports of squill-associated cardiac toxicity resulting from the abuse of opiate squill linctus (Gee's linctus).[1,2]

1. Thurston D, Taylor K. Gee's linctus. *Pharm J* 1984; **233:** 63.
2. Smith W, *et al.* Wenckebach's phenomenon induced by cough linctus. *BMJ* 1986; **292:** 868.

Preparations

BP 2008: Camphorated Opium Tincture; Concentrated Camphorated Opium Tincture; Opium Tincture;
Ph. Eur.: Opium Dry Extract, Standardised; Opium Tincture, Standardised;
USP 31: Opium Tincture; Paregoric.

Proprietary Preparations (details are given in Part 3)
Braz.: Elixir Paregorico.

Multi-ingredient: ***Braz.:*** Camomila; Elixir de Marinheiro†; ***Denm.:*** Pectyl; ***Fin.:*** Tannopon; ***Fr.:*** Colchimax; Lamaline; Paregorique; ***Hong Kong:*** Brown Mixture; ***Israel:*** Davilla; Doveri; ***Mex.:*** Reglosedyl†; ***S.Afr.:*** Paragoriese-Elikser; Tandpyndruppels; ***Spain:*** Digestovital†; Tanagel; ***Switz.:*** Bromocod N; Pectocalmine; ***USA:*** B & O Supprettes No. 15A; B & O Supprettes No. 16A; ***Venez.:*** Atrobel.

Hydrochlorides of Mixed Opium Alkaloids

Alkaloidosum Opii Hydrochloridum; Extractum Concentratum Opii; Mezclas de hidrocloruros de alcaloides del opio; Omnoponum; Opialum; Opium Concentratum.

Гидрохлориды Смешанных Алкалоидов Опия

Pharmacopoeias. Preparations of the hydrochlorides of mixed opium alkaloids are included in *Jpn.*

Papaveretum *(BAN)*

A mixture of 253 parts of morphine hydrochloride, 23 parts of papaverine hydrochloride, and 20 parts of codeine hydrochloride.

Папаверетум

CAS — 8002-76-4.
ATC — N02AA10.
ATC Vet — QN02AA10.

NOTE. Do not confuse papaveretum with papaverine (p.2191).

Pharmacopoeias. In *Br.*
BP 2008 (Papaveretum). It contains 80.0 to 88.4% of anhydrous morphine hydrochloride, 8.3 to 9.2% of papaverine hydrochloride, and 6.6 to 7.4% of anhydrous codeine hydrochloride. A white or almost white crystalline powder. Soluble in water, sparingly soluble in alcohol. A 1.5% solution in water has a pH of 3.7 to 4.7. Protect from light.

Profile

The opium alkaloids are the prototypical opioid analgesics (p.101). Mixtures of opium alkaloids such as papaveretum have the analgesic and sedative properties of morphine (p.89) and are used in the treatment of moderate to severe pain including postoperative and severe chronic pain. They may also be used for pre-operative sedation and as an adjunct to anaesthesia. Papaveretum (BP 2008) 15.4 mg contains the equivalent of about 10 mg of the major component, anhydrous morphine.

- In the UK, papaveretum formerly contained the hydrochlorides of morphine, codeine, noscapine, and papaverine. However, because of concern over the potential genotoxicity of noscapine (p.1566) UK preparations containing papaveretum were reformulated to exclude the noscapine component and the name papaveretum was redefined in the BP 1993 to reflect this change of formulation. It is possible that in other countries the term papaveretum is still being used to describe a mixture containing noscapine.

Doses. Papaveretum is generally given by subcutaneous or intramuscular injection in doses of 7.7 to 15.4 mg every 4 hours if necessary. The initial dose in the elderly or debilitated patients should not exceed 7.7 mg.

In the treatment of pain and as an adjunct in anaesthesia, papaveretum may also be given intravenously in doses of one-quarter to one-half the corresponding subcutaneous or intramuscular dose. For pre-operative medication papaveretum is given intramuscularly or subcutaneously sometimes with hyoscine hydrobromide.

For details of doses in children, see below.

Oral preparations containing papaveretum with aspirin have been given for the management of moderate to severe pain.

◊ Papaveretum has been confused with papaverine (p.2191) and in one such case[1] a patient became unconscious after self-injection of papaveretum in mistake for papaverine.

1. Robinson LQ, Stephenson TP. Self injection treatment for impotence. *BMJ* 1989; **299:** 1568.

Administration in children. Papaveretum may be given to children in the treatment of moderate to severe pain including postoperative and severe chronic pain. It is also used for pre-operative sedation and as an adjunct to anaesthesia. Papaveretum is generally given by subcutaneous or intramuscular injection every 4 hours if necessary, according to age as follows:

- neonates: 115 micrograms/kg
- 1 to 12 months: 154 micrograms/kg
- 1 to 6 years: 1.93 to 3.85 mg
- 6 to 12 years: 3.85 to 7.7 mg

Older children may be given the usual adult dose (see above).

In the treatment of pain and as an adjunct to anaesthesia papaveretum may also be given intravenously in doses of one-quarter to one-half the corresponding subcutaneous or intramuscular dose.

Preparations

BP 2008: Papaveretum Injection.

Proprietary Preparations (details are given in Part 3)
S.Afr.: Omnopon.

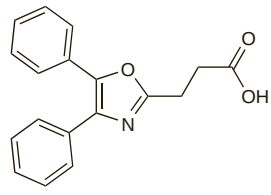
Multi-ingredient: ***UK:*** Aspav.

Oxaprozin *(BAN, USAN, rINN)*

Oksaprotsiini; Oxaprozina; Oxaprozine; Oxaprozinum; Wy-21743. 3-(4,5-Diphenyloxazol-2-yl)propionic acid.

Оксапрозин

$C_{18}H_{15}NO_3$ = 293.3.
CAS — 21256-18-8.
ATC — M01AE12.
ATC Vet — QM01AE12.



Pharmacopoeias. In *Chin.*, *Jpn.*, and *US*.
USP 31 (Oxaprozin). A white to yellowish-white, crystalline powder. Store in airtight containers at a temperature of 20° to 25°. Protect from light.

Adverse Effects, Treatment, and Precautions

As for NSAIDs in general, p.96.

Diagnosis and testing. False-positive results for testing of benzodiazepines in urine have been reported in patients taking oxaprozin.[1] The manufacturer[2] has commented that the interaction occurs with some immunoassay tests and that thin-layer chromatography can successfully discriminate between benzodiazepines and oxaprozin. False-positive results for a fluorescence polarisation immunoassay for phenytoin have also been reported in patients receiving oxaprozin.[3]

1. Pulini M. False-positive benzodiazepine urine test due to oxaprozin. *JAMA* 1995; **273:** 1905.
2. Raphan H, Adams MH. False-positive benzodiazepine urine test due to oxaprozin. *JAMA* 1995; **273:** 1905–6.
3. Patel T, *et al.* Assay interaction between oxaprozin and phenytoin. *Ann Pharmacother* 1997; **31:** 254.