5. Burdock GA. Review of the biological properties and toxicity of bee propolis (propolis). *Food Chem Toxicol* 1998; **36:** 347–63.
6. Lieberman HD, *et al.* Allergic contact dermatitis to propolis in a violin maker. *J Am Acad Dermatol* 2002; **46** (suppl): S30–S31.
7. Giusti F, *et al.* Sensitization to propolis in 1255 children undergoing patch testing. *Contact Dermatitis* 2004; **51:** 255–8.
8. Walgrave SE, *et al.* Allergic contact dermatitis from propolis. *Dermatitis* 2005; **16:** 209–15.
9. Majiene D, *et al.* Antifungal and antibacterial activity of propolis. *Curr Nutr Food Sci* 2007; **3:** 304–8.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Propoleos; ***Austral.:*** Helastop†; ***Chile:*** Propolkit; ***Ger.:*** Propolisept-Salbe; ***Ital.:*** Golapiol; Oral Spray; Pro-30C†; Pro-Gola; Propociclina; Propolcream; ***Pol.:*** Apizel; Propolan; Propolisan; Propolisol; ***USA:*** Probax.

Multi-ingredient: ***Braz.:*** Calmatoss†; Infantoss†; Malvatricin Natural Organic; Proplax†; ***Fr.:*** Pollen Royal†; Propargile; ***Ital.:*** Actires; Altuss; Apistress; Biogreen; Bodyguard; Fosfarsile Forte; Golapiol C; Immumil Plus; Immumil†; Keratolip; Neo-Stomygen; Nepiros; Otosan Natural Ear Drops†; Probigol; Promix 3†; Promix†; Propast; Propomill†; Valda Propoli; ***Switz.:*** Osa gel dentaire aux plantes; ***UK:*** Sinose.

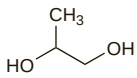
Propylene Glycol

E1520; Glicol Propilênico; Glikol propylenowy; Propilenglicol; Propilénglikol; Propilenglikolis; Propilenoglicol; Propyleeniglykoli; Propylèneglycol; Propylenglycolum; Propylenglykol. (±)-Propane-1,2-diol.

$C_3H_8O_2$ = 76.09.

CAS — 57-55-6 ((±)-propylene glycol); 4254-16-4 ((±)-propylene glycol); 4254-14-2 ((–)-propylene glycol); 4254-15-3 ((+)-propylene glycol).

ATC Vet — QA16QA01.



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

Ph. Eur. 6.2 (Propylene Glycol). A clear, colourless, viscous, hygroscopic liquid. Miscible with water and with alcohol. Store in airtight containers.

USP 31 (Propylene Glycol). A clear, colourless, practically odourless, viscous liquid. It absorbs moisture when exposed to moist air. Miscible with water, with acetone, and with chloroform; soluble in ether; will dissolve in many essential oils but is immiscible with fixed oils. Store in airtight containers.

Adverse Effects and Precautions

Systemic toxicity of propylene glycol is considered to be low after oral doses unless large quantities have been ingested, or when preparations containing propylene glycol are given to neonates or to patients in renal failure. Systemic toxicity is manifested most commonly by CNS depression, especially in neonates and children. Other reported adverse effects include hepatic or renal impairment, intravascular haemolysis, seizures, coma, arrhythmias, and cardiorespiratory arrest. Hyperosmolality has occurred, particularly in small infants and in patients with renal impairment; lactic acidosis may also be a greater problem in the latter group.

After topical use, propylene glycol may produce some local irritation, particularly if applied under occlusive dressings or to mucous membranes; toxicity may occur on application to burns. Hypersensitivity reactions have also been reported. Local sensitivity has been reported after use of ear drops with a propylene glycol vehicle. Injections of preparations containing high concentrations of propylene glycol may produce pain or irritation.

Lactic acidosis. Lactic acidosis developed in a patient with normal renal function given a high-dose continuous lorazepam infusion for which propylene glycol was the principal diluent.[1] Despite temporary resolution of symptoms when the infusion was stopped and bicarbonate given, the patient eventually died. A prospective observational pilot study[2] found propylene glycol to be a common cause of metabolic disturbances in intensive care patients receiving intravenous benzodiazepines, and the authors recommended close monitoring of all such patients.

1. Neale BW, *et al.* Propylene glycol-induced lactic acidosis in a patient with normal renal function: a proposed mechanism and monitoring recommendations. *Ann Pharmacother* 2005; **39:** 1732–6.
2. Wilson KC, *et al.* Propylene glycol toxicity: a severe iatrogenic illness in ICU patients receiving IV benzodiazepines: a case series and prospective, observational pilot study. *Chest* 2005; **128:** 1674–81.

Interactions

Anticoagulants. Propylene glycol has been reported to decrease the effect of *heparin*.[1]

1. Col J, *et al.* Propylene glycol-induced heparin resistance during nitroglycerin infusion. *Am Heart J* 1985; **110:** 171–3.

Pharmacokinetics

Propylene glycol is rapidly absorbed from the gastrointestinal tract. There is evidence of topical absorption when applied to damaged skin.

It is extensively metabolised in the liver primarily by oxidation to lactic and pyruvic acid and is also excreted in the urine unchanged.

◊ References.

1. Yu DK, *et al.* Pharmacokinetics of propylene glycol in humans during multiple dosing regimens. *J Pharm Sci* 1985; **74:** 876–9.
2. Speth PAJ, *et al.* Propylene glycol pharmacokinetics and effects after intravenous infusion in humans. *Ther Drug Monit* 1987; **9:** 255–8.

Uses and Administration

Propylene glycol is widely used in pharmaceutical manufacturing as a solvent and vehicle, especially for drugs unstable or insoluble in water. It may also be used as a stabiliser in vitamin preparations, as a plasticiser, and as a preservative. Propylene glycol is used extensively in foods and cosmetics.

Propylene glycol has humectant properties and is used similarly to glycerol in topical moisturising preparations.

Propylene glycol is used in veterinary medicine as a glucose precursor.

Preparations

Proprietary Preparations (details are given in Part 3)

USA: Advanced Eye Relief.

Multi-ingredient: ***Arg.:*** Systane; ***Austral.:*** Dermatech Liquid; ***Austria:*** Acerbine; ***Canad.:*** Episec; Gyne-Moistrin†; Rhinaris; Rhinedrine Moisturizing†; Salinol†; Secaris; Systane; ***Chile:*** Systane; ***Fr.:*** Intrasite; Propy-Lacticare; Systane; ***Ger.:*** Sekudrill†; ***Hong Kong:*** Moisture Eyes; Systane; ***Israel:*** Pedisol†; Taro Gel; ***Ital.:*** Dopo Pik; Sekudrill; Systane; ***Malaysia:*** Systane; ***Mex.:*** Moisture Eyes; Systane; ***Philipp.:*** Moisture Eyes; Systane; ***S.Afr.:*** Aserbine; ***Singapore:*** Systane; ***Spain:*** Acerbiol; ***Switz.:*** Acerbine†; ***Thai.:*** Systane; ***UK:*** Aserbine†; ***USA:*** Astroglide; Biotene with Calcium; Surgel; Zonite; ***Venez.:*** Systane.

Prostaglandins

Profile

The prostaglandins, along with thromboxanes and leukotrienes, are all derived from 20-carbon polyunsaturated fatty acids and are collectively termed *eicosanoids*. In man, the most common precursor is arachidonic acid (eicosatetraenoic acid) whereas eicosapentaenoic acid is a predominant precursor in fish and marine animals.

Arachidonic acid is released from cell-membrane phospholipids by the enzyme phospholipase A_2 and is then rapidly metabolised by several enzymes, the major ones being cyclo-oxygenase (prostaglandin synthetase) and lipoxygenase (see Figure 1, below). The prostaglandins, thromboxanes, and prostacyclin (sometimes collectively termed *prostanoids*) all contain ring structures and are products of arachidonic acid oxidation by cyclo-oxygenase, an enzyme with 2 isoforms (COX-1 or COX-2) widely distributed in cell membranes.

The leukotrienes are products of the lipoxygenase pathway; arachidonic acid is metabolised by lipoxygenases to hydroperoxyeicosatetraenoic acids, which are then further metabolised to leukotrienes.

The initial step in the cyclo-oxygenase pathway is the formation of cyclic endoperoxide prostaglandin G_2 (PGG_2) which is then reduced to the endoperoxide prostaglandin H_2 (PGH_2). Prostaglandin H_2 is then converted to the primary prostaglandins prostaglandin D_2, prostaglandin E_2, and prostaglandin F_2 , to thromboxane A_2 (TXA_2) via the enzyme thromboxane synthetase, or to prostacyclin (PGI_2) via the enzyme prostacyclin synthetase. These products are further metabolised and rapidly inactivated in the body.

The secondary prostaglandins, prostaglandin A_2 (PGA_2), prostaglandin B_2 (PGB_2), and prostaglandin C_2 (PGC_2) are derived from prostaglandin E_2, but are formed during extraction and probably do not occur biologically.

The prostaglandins are all derivatives of the carbon skeleton 7-(2-octilcyclopentyl)heptanoic acid (also known as prostanoic acid). All natural prostaglandins have a double bond at position 1,2 and a hydroxyl group at position 3 of the octil side-chain. Depending on the substitutions on the cyclopentane ring, the main series of prostaglandins are distinguished by the letters A, B, C, D, E, and F; the members of each series are further subdivided by subscript numbers which indicate the degree of unsaturation in the side-chains—hence, those derived from eicosatrienoic acid (dihomo-γ-linolenic acid) have the subscript 1, those derived from arachidonic acid have the subscript 2, and those derived from eicosapentaenoic acid have the subscript 3. In man, only prostaglandins of the '2' series appear to be of physiological importance. Thromboxane A_2 has an oxane rather than a cyclopentane ring; it is chemically unstable and breaks down to thromboxane B_2. Prostacyclin has a double-ring structure and breaks down to 6-keto-prostaglandin F_1 .

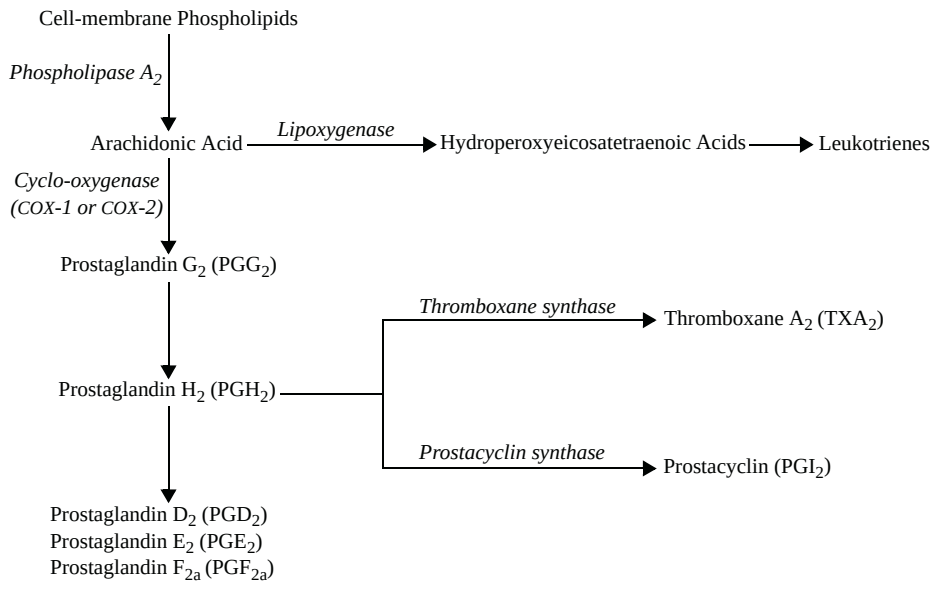
Endogenous prostaglandins are autacoids; they can be formed by virtually all tissues and cells in response to a variety of stimuli, have a wide range of **actions**, and are involved in the regulation of virtually all biological functions. Prostaglandins appear to act through various receptor-mediated mechanisms. Some of their effects are mediated within cells by activation or inhibition of adenylate cyclase and the regulation of cyclic adenosine monophosphate production. At one time prostaglandin E_2 and prostaglandin F_2 were thought to be of paramount importance, but with the discovery of thromboxane A_2, prostacyclin, and the leukotrienes it was realised that these primary prostaglandins belong to a large family of physiologically active eicosanoids. Thromboxane A_2 induces platelet aggregation and constricts arterial smooth muscle whereas prostacyclin causes vasodilatation and prevents platelet aggregation; the balance between these opposing actions has an important role in the regulation of intravascular platelet aggregation and thrombus formation. The leukotrienes are important mediators of inflammation.

The pharmacological properties of prostaglandins are wide-ranging and include contraction or relaxation of smooth muscle in the blood vessels, bronchi, uterus, and gastrointestinal tract; inhibition of gastric acid secretion; and effects on platelet aggregation, the endocrine system, and metabolic processes.

Individual prostaglandins vary greatly in their activities and potencies; their actions also depend on the animal species, on the tissues in which they are acting, and on the concentration present, and entirely opposite actions may be elicited with very small structural changes in the molecule.

The diverse **clinical applications** of prostaglandins reflect their wide-ranging physiological and pharmacological properties. Synthetic analogues have been developed with the aim of obtain-

Figure 1. Prostaglandin biosynthesis.



ing compounds that are more stable, have a longer duration of action, and a more specific effect. Applications include:

- softening and dilating the cervix and for uterine stimulation, e.g. dinoprost (prostaglandin F_2) (p.2006) and its analogue carboprost (p.2006); dinoprostone (prostaglandin E_2) (p.2007) and its analogue sulprostone (p.2018); and gemeprost (p.2010) and misoprostol (p.2013), analogues of prostaglandin E_1
- vasodilators and inhibitors of platelet aggregation, e.g. alprostadil (prostaglandin E_1) (p.2183) and its analogue limaprost (p.1325); and epoprostenol (prostacyclin) (p.1279) and its analogue iloprost (p.1313)
- inhibition of gastric acid secretion and protection of the gastrointestinal mucosa, e.g. misoprostol (p.2013)
- glaucoma treatment, e.g. bimatoprost (p.1878), latanoprost (p.1882), travoprost (p.1886), and unoprostone (p.1886)
- as luteolytics (causing regression of the corpus luteum in the ovary) in veterinary medicine, e.g. synthetic analogues of prostaglandin F_2 .

◊ References.

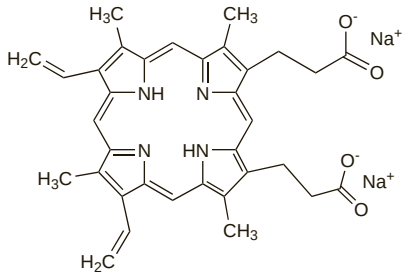
1. Moncada S, Vane JR. Arachidonic acid metabolites and the interactions between platelets and blood-vessel walls. *N Engl J Med* 1979; **300:** 1142–7.
2. Higgs GA, Vane JR. Inhibition of cyclo-oxygenase and lipoxygenase. *Br Med Bull* 1983; **39:** 265–70.
3. Halushka PV, *et al.* Thromboxane, prostaglandin and leukotriene receptors. *Annu Rev Pharmacol Toxicol* 1989; **29:** 213–39.
4. Smith WL, *et al.* Prostaglandin and thromboxane biosynthesis. *Pharmacol Ther* 1991; **49:** 153–79.
5. O'Neill C. The biochemistry of prostaglandins: a primer. *Aust N Z J Obstet Gynaecol* 1994; **34:** 332–7.
6. Wu KK. Molecular regulation and augmentation of prostacyclin biosynthesis. *Agents Actions Suppl* 1995; **45:** 11–17.

Protoporphyrin IX Disodium

Protoporfirina IX disódica; Protoporphyrin Disodium. Disodium 7,12-diethenyl-3,8,13,17-tetramethyl-21*H*,23*H*-porphine-2,18-dipropanoate.

$C_{34}H_{32}N_4Na_2O_4$ = 606.6.

CAS — 50865-01-5 (protoporphyrin IX disodium); 553-12-8 (protoporphyrin IX).



Profile

Protoporphyrin IX disodium has been given by mouth for the treatment of impaired hepatic function associated with gallstones and cholecystitis.

Proxazole Citrate *(USAN, rINNM)*

AF-634; Citrato de proxazol; Propaxoline Citrate; Proxazole, Citrate de; Proxazoli Citras; PZ-17105. *NN*-Diethyl-3-(1-phenylpropyl)-1,2,4-oxadiazole-5-ethanamine citrate.

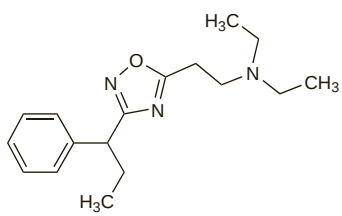
Проксазола Цитрат

$C_{17}H_{25}N_3O,C_6H_8O_7$ = 479.5.

CAS — 5696-09-3 (proxazole); 132-35-4 (proxazole citrate).

ATC — A03AX07.

ATC Vet — QA03AX07.



(proxazole)

Profile

Proxazole citrate has been used as an antispasmodic and in vascular disorders.

Preparations

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

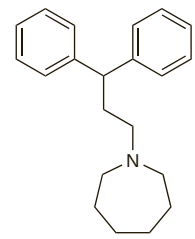
Prozapine Hydrochloride *(rINNM)*

Hexadiphane Hydrochloride; Hidrocloruro de prozapina; Prozapine, Chlorhydrate de; Prozapini Hydrochloridum. 1-(3,3-Diphenylpropyl)cyclohexamethyleneimine hydrochloride.

Прозапина Гидрохлорид

$C_{21}H_{27}N,HCl$ = 329.9.

CAS — 3426-08-2 (prozapine); 13657-24-4 (prozapine hydrochloride).



(prozapine)

Profile

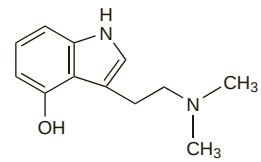
Prozapine hydrochloride is an antispasmodic that has been given orally with sorbitol in biliary and gastrointestinal disorders.

Psilocin

4-Hydroxy-*NN*-dimethyltryptamine; Psilocina; Psilocyn. 3-(2-Dimethylaminoethyl)indol-4-ol.

$C_{12}H_{16}N_2O$ = 204.3.

CAS — 520-53-6.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of psilocin or mushrooms containing psilocin:
1UP's; Abhort; Aborts; Alice; Benzies; Blue Rimmers; Boom-Dads; Boomers; Caps; Crumb Tarts; Cubes; FireWorks; Fun Gus; Fun Guys; Fungus; God's flesh; Goombas; Gus; Jesus; Lalkas; Liberty caps; Little smoke; Magic mushroom; Magic Mushrooms; Marios; Mexican mushroom; Mexican mushrooms; Mucks; Muggers; Mush; Mushies; Mushrooms; Musk; Pizza Toppings; Shroomies; Shrooms; Silly putty; Simple Simon; Smurfhats; Toads; Umbrellas; Yellow Bentines; Zoomers; Zoomies.

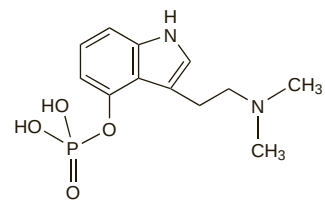
Psilocybine *(BAN, rINN)*

CY-39; 4-Phosphoryloxy-*NN*-dimethyltryptamine; Psilocibina; Psilocybin; Psilocybinum; Psilosybiini. 3-(2-Dimethylaminoethyl)indol-4-yl dihydrogen phosphate.

Псилоцибин

$C_{12}H_{17}N_2O_4P$ = 284.2.

CAS — 520-52-5.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of psilocybine or mushrooms containing psilocybine:
1 UP's; Alice; Benzies; Blue caps; Blue Rimmers; Boom-Dads; Boomers; Booms; Buttons; Caps; Champ; Crumb Tarts; Cubes; FireWorks; Fun Gus; Fun Guys; Fungus; Funguys; God's flesh; Goombas; Gus; Hombrecitos; Jesus; Lalkas; Las mujercitas; Little smoke; Magic mushroom; Magic mushrooms; Marios; Mexican mushroom; Mexican mushrooms; Mucks; Muggers; Mush; Mushies; Mushroom soup; Mushroom tea; Mushrooms; Musk; Philosopher's Stones; Pizza toppings; Rooms; Sacre mushroom; Sacred mushroom; Sacred mushrooms; Shroomies; Shrooms; Silly putty; Simple Simon; Smurfhats; Teonanactl; Toads; Truffles; Umbrellas; Yellow Bentines; Zoomers; Zoomies.

Profile

Psilocin and psilocybine are indole alkaloids obtained from the sacred Mexican mushroom (teonanácatl), *Psilocybe mexicana* (Agaricaceae).

In the UK, psilocybine is present in the indigenous mushroom *Psilocybe semilanceata* (magic mushroom; liberty cap). Psilocybine is also present in other species of mushrooms including *Stropharia cubensis* and *Conocybe* spp.

Psilocybine has hallucinogenic and sympathomimetic properties similar to those of lysergide (p.2335). It is less potent than lysergide and its hallucinogenic effects last for up to 6 hours. There is evidence to suggest that psilocybine is converted to the active form psilocin in the body. It has no therapeutic use.

Pulegium Oil

Pennyroyal Oil; Poleo, aceite esencial de.

Profile

Pulegium oil is a volatile oil distilled from pennyroyal herb, *Mentha pulegium* (Labiatae), containing pulegone ($C_{10}H_{16}O$ = 152.2). It was formerly used as an emmenagogue. Severe toxic effects have followed its use as an abortifacient with convulsions, hepatotoxicity, and death. It is reported to have insect repellent activity.

Adverse effects. Severe hepatotoxicity accompanied by seizures occurred in 2 infants each of whom had received herbal teas containing pulegium oil.[1] In one of the infants multiple organ failure developed, and fulminant hepatic failure with hepatocellular necrosis and cerebral oedema proved fatal. A further 4 cases of toxicity associated with ingestion of pulegium oil have been reported;[2] three of the cases were adult patients who had ingested either herbal teas to induce menses (2 cases) or a herbal extract as an abortifacient (1 fatality), and the fourth was a 22-month old child who had ingested the oil.

1. Bakerink JA, *et al.* Multiple organ failure after ingestion of pennyroyal oil from herbal tea in two infants. *Pediatrics* 1996; **98:** 944–7.
2. Anderson IB, *et al.* Pennyroyal toxicity: measurement of toxic metabolite levels in two cases and review of the literature. *Ann Intern Med* 1996; **124:** 726–34.

Pulmonary Surfactants

Tensioactivos pulmonares.

Description. Pulmonary surfactants are mixtures consisting mainly of phospholipids and surfactant proteins that are used to replace deficient endogenous lung surfactants. A number of preparations have been studied including:

- natural human surfactant obtained from amniotic fluid or biosynthetic material
- natural animal-derived surfactants, which are bovine or porcine lung extracts that may be modified by the addition of synthetic surfactants, as in the case of beractant, or unmodified, as in the case of bovactant and calfactant
- synthetic or semisynthetic preparations, which may contain the phospholipid colfosceril palmitate, a major constituent of natural lung surfactants, in combination with other substances that aid spreading and absorption such as the synthetic peptide sinapultide.

Beractant *(BAN, USAN)*

A-60386X.

CAS — 108778-82-1.

Description. Beractant is a modified bovine lung extract containing mostly phospholipids, modified by the addition of colfosceril palmitate, palmitic acid, and tripalmitin.
The term Surfactant TA has been applied to a modified bovine lung surfactant.

Bovactant *(BAN)*

SF-R11.

Description. Bovactant is an extract of bovine lung containing about 92% of phospholipids, 3.2% of cholesterol, 0.6% of surfactant-associated hydrophobic proteins, and 0.4% of free fatty acid.

Calfactant *(BAN, USAN)*

CAS — 183325-78-2.

Description. Calfactant is an unmodified calf lung extract that includes mostly phospholipids and hydrophobic surfactant-specific proteins (SP-B and SP-C).