

## Preparations

**Proprietary Preparations** (details are given in Part 3)

**Multi-ingredient:** **S.Afr.:** Bolus Eucalypti Comp; **Switz.:** Forapinj†.

## Apricot

**Pharmacopoeias.** *Chin.* includes Bitter Apricot Seed, the kernel obtained from various species of *Prunus*. *Jpn* includes a monograph for Apricot Kernel.

## Profile

The kernels of the apricot, *Prunus armeniaca* (*Armeniaca vulgaris*; *P. tiliifolia*) (Rosaceae), are used in Chinese medicine for disorders of the respiratory tract and for constipation.

Apricot is a source of persic oil (p.2365). Amygdalin, the major cyanogenic glycoside of apricot kernels, is the major constituent of laetrile (p.2330). Apricot kernels are also a source of pangamic acid (p.2362).

Apricot fruits are used as a food.

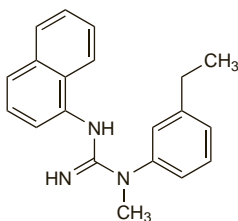
## Aptiganel (pINN)

Aptiganelum. 1-(*m*-Ethylphenyl)-1-methyl-3-(1-naphthyl)guanidine.

Аптиганел

C<sub>20</sub>H<sub>21</sub>N<sub>3</sub> = 303.4.

CAS — 137159-92-3.



## Aptiganel Hydrochloride (USAN)

CNS-1102.

C<sub>20</sub>H<sub>21</sub>N<sub>3</sub>.HCl = 339.9.

CAS — 137160-11-3.

## Profile

Aptiganel is a guanidine derivative that antagonises the effects of the excitatory amino-acid neurotransmitter glutamate at NMDA-receptors. It has been investigated for the prevention of ischaemic brain damage in patients with traumatic head injury or stroke.

◇ Following dose-ranging studies of aptiganel in healthy subjects<sup>1</sup> and in patients,<sup>2</sup> adverse effects reported<sup>3</sup> in patients with acute ischaemic stroke, at doses that had been neuroprotective in *animals*, included an increase in systolic blood pressure and an excess of CNS effects. A randomised controlled study<sup>4</sup> in patients with acute ischaemic stroke was suspended because of a lack of efficacy and a potential imbalance in mortality compared with placebo.

- Muir KW, *et al.* Pharmacological effects of the non-competitive NMDA antagonist CNS 1102 in normal volunteers. *Br J Clin Pharmacol* 1994; **38**: 33–8.
- Block GA, *et al.* Final results from a dose-escalating safety and tolerance study of the non-competitive NMDA antagonist CNS1102 in patients with acute cerebral ischaemia. *Stroke* 1995; **26**: 185.
- Dyker AG, *et al.* Safety and tolerability study of aptiganel hydrochloride in patients with an acute ischemic stroke. *Stroke* 1999; **30**: 2038–42.
- Albers GW, *et al.* Aptiganel hydrochloride in acute ischemic stroke: a randomized controlled trial. *JAMA* 2001; **286**: 2673–82.

## Arachis Oil

Arachide, huile d', raffinée; Arachidis Oleum; Arachidis oleum raffinatium; Cacahuete, aceite de; Earth-nut Oil; Erdnussöl; Finonitott földimogyoróolaj; Ground-nut Oil; Huile d'Arachide; Jordnötolja, raffinerad; Maapähkinäöljy, puhdistettu; Nut Oil; Ol. Arach.; Olej arachidowy oczyszczony; Oleo de Amendoim; Oleum Arachis; Peanut Oil; Podzemnicový olej čistěný; Refined Arachis Oil; Yerfistigi; Yağı; Žemės riešutų aliejus.

**Pharmacopoeias.** In *Eur.* (see p.vii), *Int.*, and *Jpn.* Also in *US-NF*.

*Eur.* also includes hydrogenated arachis oil.

**Ph. Eur. 6.2** (Arachis Oil, Refined; Arachis Oil BP 2008). The refined fatty oil obtained from the shelled seeds of *Arachis hypogaea*. A suitable antioxidant may be added. It is a clear, yellowish viscous liquid consisting of glycerides, chiefly of oleic and linoleic acids, with smaller amounts of other acids. It solidifies at

about 2°. Very slightly soluble in alcohol; miscible with petroleum spirit. Store in well-filled containers. Protect from light.

The BP 2008 gives Ground-nut Oil and Peanut Oil as approved synonyms.

**Ph. Eur. 6.2** (Arachis Oil, Hydrogenated; Arachidis Oleum Hydrogenatum). Arachis oil that has been refined, bleached, hydrogenated, and deodorised. It is a white or faintly yellowish soft mass that melts to a clear pale yellow liquid when heated. Practically insoluble in water; very slightly soluble in alcohol; freely soluble in dichloromethane and in petroleum spirit (b.p. 65° to 70°). Protect from light.

**USNF 26** (Peanut Oil). The fully-refined (alkali-refined, bleached, and deodorised at 230° to 260°) oil obtained from the seed kernels of one or more of the cultivated varieties of *Arachis hypogaea* (Leguminosae). It is a colourless or pale yellow, oily liquid with a bland taste; it may have a characteristic nutty odour. Very slightly soluble in alcohol; miscible with carbon disulfide, with chloroform, and with ether. Store at a temperature not exceeding 40° in airtight containers. Protect from light.

## Profile

Emulsions containing arachis oil are used in nutrition. Arachis oil is given as an enema for softening impacted faeces. It is used in drops for softening ear wax (see under Docusates, p.1725) and in emollient creams. Arachis oil is given by mouth, usually with sorbitol, as a gallbladder evacuant prior to cholecystography.

**Precautions.** It has been suggested that the use during infancy of preparations containing arachis oil, including infant formulae and topical preparations, may be responsible for sensitisation to peanut, with a subsequent risk of hypersensitivity reactions.<sup>1-3</sup> The arachis oil used in such preparations is refined oil and it has been pointed out that such oil should not contain the proteins that produce allergic reactions in susceptible people.<sup>4,5</sup> In the USA, heating of arachis oil during preparation, to further reduce protein content, has been proposed.<sup>6</sup> Nonetheless, some consider that sufficient protein may be present in refined oil to cause sensitisation.<sup>7</sup> However, others have pointed out that to date, there are no reliable data about doses of topical arachis oil needed to induce sensitisation via the epidermal route and that the benefit of protecting skin barrier functions in atopic patients with products using refined arachis oil outweigh possible risks of sensitisation.<sup>8</sup> In the UK, the CSM considered that there was not enough evidence to conclude that medicinal products containing arachis oil could lead to sensitisation.<sup>9</sup> However, although they considered the risk of a reaction to be low, they recommended that patients known to be allergic to peanuts should not use medicines containing arachis oil (nor, because of the possibility of cross-sensitivity, should patients allergic to soya), and that such medicines should include an appropriate warning in the labelling.

- de Montis G, *et al.* Sensitisation to peanut and vitamin D oily preparations. *Lancet* 1993; **341**: 1411.
- Lever LR. Peanut and nut allergy: creams and ointments containing peanut oil may lead to sensitisation. *BMJ* 1996; **313**: 299.
- Lack G, *et al.* Factors associated with the development of peanut allergy in childhood. *N Engl J Med* 2003; **348**: 977–85.
- Hourihane J O'B, *et al.* Randomised, double blind, crossover challenge study of allergenicity of peanut oil in subjects allergic to peanuts. *BMJ* 1997; **314**: 1084–8.
- Committee on Toxicity of chemicals in Food, Consumer Products and the Environment. *Peanut allergy*. London: Department of Health, 1998.
- Wilkin JK, *et al.* Peanut allergy. *N Engl J Med* 2003; **349**: 302.
- Lack G, *et al.* Peanut allergy. *N Engl J Med* 2003; **349**: 302–3.
- Ring J, Möhrenschrager M. Allergy to peanut oil — clinically relevant? *J Eur Acad Dermatol Venereol* 2007; **21**: 452–5.
- Committee on Safety of Medicines/Medicines and Healthcare Regulatory Agency. Medicines containing peanut (arachis) oil. *Current Problems* 2003; **29**: 5. Also available at: [http://www.mhra.gov.uk/home/idcplg?IdcService=GET\\_FILE&DocName=CON007450&RevisionSelectionMethod=LatestReleased](http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&DocName=CON007450&RevisionSelectionMethod=LatestReleased) (accessed 14/07/06)

## Preparations

**BP 2008:** Arachis Oil Enema.

**Proprietary Preparations** (details are given in Part 3)

**Austral.:** Calogen; **Chile:** Oilatun; **Denm.:** Olie; **Fin.:** Calogen; **Ger.:** Olbad Cordes F; **Indon.:** Oilatun Cream; **Irl.:** Calogen; Fletcher's Arachis Oil; Oilatun Cream; **Ital.:** Calogen; **Mex.:** Dermo Bell; Nutrisil; Oilatun; **NZ:** Calogen; **S.Afr.:** Oilatun Cream; **Singapore:** Oilatun Cream; **UK:** Calogen; Fletcher's Arachis Oil Retention Enema†.

**Multi-ingredient:** **Austral.:** Cerumol; Gold Cross Skin Basics Zinc Cream†; Medevac†; **Austria:** Balneum F; **Chile:** Tarytar†; **Cz.:** Balneum Hermal F; **Ger.:** Balneum F; Parfenac Basisbad†; **Irl.:** Cerumol; Hydromol†; **Israel:** Balneum F; Cerumol; **Ital.:** Balneum Hermal Forte; **NZ:** Medevac†; **Pol.:** Balneum Hermal F; **S.Afr.:** Cerumol; Haarlemensis; **Singapore:** Cerumol; **Spain:** Emolytar; **Switz.:** Balméd Hermal F; Balneum Hermal F†; **UK:** Cerumol; Earex; Hewletts; Nowax; Red Oil; Soothol.

## Areca

Areca Nuts; Arecae Semen; Arekasame; Betel; Betel Nuts; Noix d'Areca.

**NOTE.** The following terms have been used as 'street names' (see p.vi) or slang names for various forms of areca:

Daka; Gua; Maag; Mak; Marg; Pan parag; Pinang; Puguay; Puwak; Supai; Suparim.

**Pharmacopoeias.** In *Chin.* and *Jpn.*

## Profile

Areca consists of the dried ripe seeds of *Areca catechu* (Palmae) containing the alkaloid arecoline.

Areca is used in Asian countries as a masticatory. It has sialagogue properties and is chewed for its mild intoxicant and euphoriant effects. The usual custom is to chew pieces of areca seed (areca nut; betel nut) wrapped with lime (calcium hydroxide) in the leaf of the betel pepper (betelvine) (*Piper betle*, which is unrelated to areca). This preparation is known as 'betel quid' (betel) or 'paan' (pan-masala), and produces a red juice when chewed, which stains the saliva, teeth and mucosa. Other ingredients that might be added include catechu gum, spices, or tobacco.

Arecoline and arecaidine (produced by the hydrolysis of arecoline when chewed with lime) have cholinergic activity, and adverse effects that may occur with initial or heavy use of areca include excessive salivation, sweating, lachrymation, urinary incontinence, or diarrhoea. An increased incidence of oral submucosal fibrosis, oral leucoplakia, and oral squamous cell carcinoma has been reported following habitual use.

Areca was formerly used in the treatment of tapeworm infection, and arecoline has been used in veterinary medicine as a purgative and taenifuge.

◇ Discussions of the health risks associated with the chewing of preparations containing areca nut by indigenous populations in Asia<sup>1-3</sup> and immigrant groups in the UK,<sup>4</sup> USA,<sup>5</sup> and New Zealand,<sup>6</sup> including acute effects.<sup>2,3,5</sup> See also Adverse Effects of Tobacco Products under Nicotine (p.2352) for reference to mixtures of areca and tobacco.

- Mack TM. The new pan-Asian paan problem. *Lancet* 2001; **357**: 1638–9.
- Deng JF, *et al.* Acute toxicities of betel nut: rare but probably overlooked events. *J Toxicol Clin Toxicol* 2001; **39**: 355–60.
- Chu NS. Effects of Betel chewing on the central and autonomic nervous systems. *J Biomed Sci* 2001; **8**: 229–36.
- Warnakulasuriya S, *et al.* Areca nut use: an independent risk factor for oral cancer. *BMJ* 2002; **324**: 799–800.
- Nelson BS, Heischouer B. Betel nut: a common drug used by naturalized citizens from India, Far East Asia, and the South Pacific Islands. *Ann Emerg Med* 1999; **34**: 238–43.
- Yoganathan P. Betel chewing creeps into the New World. *N Z Dent J* 2002; **98**: 40–5.

**Carcinogenicity.** Precancerous and cancerous conditions of the oral cavity have been attributed to the chewing of preparations containing areca (see above). In betel-chewer's mucosa, the oral mucosa is discoloured and there is desquamation or peeling of the oral epithelium from the traumatic effect of chewing and possibly a chemical action of the constituents. This condition may be a precursor of oral submucosal fibrosis, which is considered to be precancerous.<sup>1</sup> Oral leucoplakia is another precancerous condition that is reported. The role of areca in the development of these conditions and oral squamous cell carcinoma has been debated. The effects may be due to the arecaidine content of areca, the alkalinity of the lime, presence of tobacco, or a combination of these.<sup>2,3</sup> Results from a case-controlled study<sup>4</sup> point to an independent association between oral squamous cell carcinoma and chewing areca seeds in preparations without tobacco compared with non-users of areca. A review<sup>5</sup> of available evidence strongly supports this association.

- Reichart PA, Philipsen HP. Betel chewer's mucosa—a review. *J Oral Pathol Med* 1998; **27**: 239–42.
- Norton SA. Betel: consumption and consequences. *J Am Acad Dermatol* 1998; **38**: 81–8.
- Nelson BS, Heischouer B. Betel nut: a common drug used by naturalized citizens from India, Far East Asia, and the South Pacific Islands. *Ann Emerg Med* 1999; **34**: 238–43.
- Merchant A, *et al.* Paan without tobacco: an independent risk factor for oral cancer. *Int J Cancer* 2000; **86**: 128–31.
- Nair U, *et al.* Alert for an epidemic of oral cancer due to use of the betel quid substitutes gutkha and pan masala: a review of agents and causative mechanisms. *Mutagenesis* 2004; **19**: 251–62.

**Effects on the lungs.** Evidence suggesting that there is an association between betel-nut chewing and bronchoconstriction in asthmatic patients.<sup>1,2</sup>

- Taylor RFH, *et al.* Betel-nut chewing and asthma. *Lancet* 1992; **339**: 1134–6.
- Kiyongi KS. Betel nut chewing and asthma. *Lancet* 1992; **340**: 59–60.

**Effects on the nervous system.** Areca-nut (betel-nut) chewing is associated with habituation, addiction, and dependence,<sup>1</sup> and CNS symptoms of withdrawal have been described in 2 patients.<sup>2</sup> A case of neonatal withdrawal syndrome in an infant born to a chronic areca-nut user has also been reported.<sup>3</sup> Psychosis has also been reported.<sup>1</sup>

It has been suggested that the muscarinic action of areca alkaloids may have a beneficial effect on symptoms of schizophrenia, and a study of such patients in a Micronesian population provides some support for this idea.<sup>4</sup> However, severe extrapyramidal symptoms followed betel-nut chewing in 2 patients with chronic schizophrenia who were also receiving antipsychotic therapy.<sup>5</sup>

- Nelson BS, Heischouer B. Betel nut: a common drug used by naturalized citizens from India, Far East Asia, and the South Pacific Islands. *Ann Emerg Med* 1999; **34**: 238–43.