Oral pimecrolimus is also under investigation and has reduced disease severity in dose-finding studies in patients with chronic plaque psoriasis.[5,6]

1. Gribetz C, *et al.* Pimecrolimus cream 1% in the treatment of intertriginous psoriasis: a double-blind, randomized study. *J Am Acad Dermatol* 2004; **51:** 731–8.
2. Mrowietz U, *et al.* The novel ascomycin derivative SDZ ASM 981 is effective for psoriasis when used topically under occlusion. *Br J Dermatol* 1998; **139:** 992–6.
3. Mrowietz U, *et al.* An experimental ointment formulation of pimecrolimus is effective in psoriasis without occlusion. *Acta Derm Venereol* 2003; **83:** 351–3.
4. Kreuter A, *et al.* 1% Pimecrolimus, 0.005% calcipotriol, and 0.1% betamethasone in the treatment of intertriginous psoriasis: a double-blind, randomized controlled study. *Arch Dermatol* 2006; **142:** 1138–43.
5. Rappersberger K, *et al.* Pimecrolimus identifies a common genomic anti-inflammatory profile, is clinically highly effective in psoriasis and is well tolerated. *J Invest Dermatol* 2002; **119:** 876–87.
6. Gottlieb AB, *et al.* Oral pimecrolimus in the treatment of moderate to severe chronic plaque-type psoriasis: a double-blind, multicentre, randomized, dose-finding trial. *Br J Dermatol* 2005; **152:** 1219–27.

Seborrhoeic dermatitis. Small studies[1,2] suggest that topical pimecrolimus has a similar efficacy to topical corticosteroids in the treatment of seborrhoeic dermatitis (p.1584). It has also been effective in a few cases that had not responded to topical corticosteroids.[3]

1. Rigopoulos D, *et al.* Pimecrolimus cream 1% vs. betamethasone 17-valerate 0.1% cream in the treatment of seborrhoeic dermatitis: a randomized open-label clinical trial. *Br J Dermatol* 2004; **151:** 1071–5.
2. Firooz A, *et al.* Pimecrolimus cream, 1%, vs hydrocortisone acetate cream, 1%, in the treatment of facial seborrheic dermatitis: a randomized, investigator-blind, clinical trial. *Arch Dermatol* 2006; **142:** 1066–7.
3. Cunha PR. Pimecrolimus cream 1% is effective in seborrhoeic dermatitis refractory to treatment with topical corticosteroids. *Acta Derm Venereol* 2006; **86:** 69–70.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Elidel; ***Austral.:*** Elidel; ***Austria:*** Elidel; ***Belg.:*** Elidel; ***Braz.:*** Elidel; ***Canad.:*** Elidel; ***Chile:*** Elidel; ***Cz.:*** Elidel; ***Denm.:*** Elidel; ***Fin.:*** Elidel; ***Fr.:*** Elidel; ***Ger.:*** Douglan; Elidel; ***Gr.:*** Aregen; Elidel; ***Hong Kong:*** Elidel; ***Hung.:*** Elidel; ***Indon.:*** Elidel; ***Israel:*** Elidel; ***Ital.:*** Elidel; ***Malaysia:*** Elidel; ***Mex.:*** Elidel; ***Neth.:*** Elidel; ***Norw.:*** Elidel; ***NZ:*** Elidel; ***Philipp.:*** Elidel; ***Pol.:*** Elidel; ***Port.:*** Aregen; Elidel; ***Rus.:*** Elidel (Элидел); ***S.Afr.:*** Elidel; ***Singapore:*** Elidel; ***Spain:*** Elidel; Isaplic; Rizan; ***Swed.:*** Elidel; ***Switz.:*** Elidel; ***Thai.:*** Elidel; ***Turk.:*** Elidel; ***UK:*** Elidel; ***USA:*** Elidel; ***Venez.:*** Elidel.

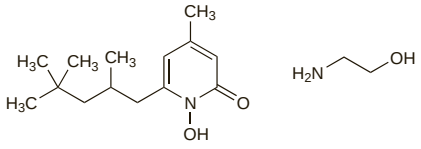
Piroctone Olamine *(USAN, rINNM)*

Piroctona olamina; Piroctoni Olaminum. 1-Hydroxy-4-methyl-6-(2,4,4-trimethylpentyl)-2(1*H*)-pyridone compound with 2-aminoethanol (1:1).

Пироктон Оламин

$C_{14}H_{23}NO_2,C_2H_7NO$ = 298.4.

CAS — 50650-76-5 (piroctone); 68890-66-4 (piroctone olamine).



Profile

Piroctone olamine has been used in shampoos for the treatment of dandruff.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Lovilia†; Megacistin G†; Octopil†; Plusgel; ***Austral.:*** Neoceuticals Therapeutic Shampoo†; ***Braz.:*** Soapex; ***Fr.:*** Charlieu Antipelliculaire; Cystel Antipelliculaire†; Evolith DS; Topicrem Traitement PV; Traitement PV; ***Irl.:*** Saliker†; ***Ital.:*** Olamin P; ***Mex.:*** Betapirox; ***Venez.:*** Betapirox; Hair Stabil†; Sante Vite†.

Multi-ingredient: ***Arg.:*** Aspergun†; Micocert; Micodual; Pitiriax; Pityval†; Saliker†; Tersoderm Anticaspa†; ***Braz.:*** Ortosol P; Pityval; Saliker; ***Chile:*** Eucerin Shampoo Anticaspa; Foltene Research Anticaspa; KPL†; Neostrata; Node DS; Shampoo Anticaspa; ***Fr.:*** Alpha 5 DS†; Epiphane†; Hyfac soin keratolytique†; Ionax P; Item Alphakeptol; Kelual DS; Kerium Intensive; Liperol; Mela'aura; Node DS; Node P; Phytheol; Phytosquame; Pityker†; Pityval; PSO; Saliker†; Seborheane; T/Gel; ***Irl.:*** Effaclar AI; ***Ital.:*** Biophase Shampoo; Biothymus DS; Genisol; Nonak; Prurex; Shamday Antiforfora†; Tricoderm F; ***Port.:*** Alpha Septol; Alphakeptol†; Bioclin Sebo Care; Ionil P†; ***Spain:*** Ionax P†; ***UK:*** Atopiclair; ***USA:*** Atopiclair; ***Venez.:*** Kertyol; Node DS; Sensibio DS.

Podophyllum

American Mandrake; May Apple Root; Podófilo; Podofilum; Podoph.; Podophyllum Rhizome; Rizoma de podófilo.

Подофилл щитовидный (*Podophyllum peltatum*)

Pharmacopoeias. In *US*.

USP 31 (Podophyllum). The dried rhizomes and roots of *Podophyllum peltatum* (Berberidaceae). It yields not less than 5% of resin. It has a slight odour.

Indian Podophyllum

Ind. Podoph.; Indian Podophyllum Rhizome; Podófilo indio.

Подофилл гималайский (*Podophyllum emodi*)

Description. The dried fruits or rhizomes and roots of *Podophyllum hexandrum* (*P. emodi*) (Berberidaceae).

Podophyllum Resin

Podofilino; Podoph. Resin; Podophylli Resina; Podophyllin; Resina de podófilo.

Подофиллин

CAS — 8050-60-0.

Pharmacopoeias. In *Int.* and *US* (both from podophyllum only). In *Br.* from Indian podophyllum.

BP 2008 (Podophyllum Resin). The resin obtained from the rhizomes and roots of *Podophyllum hexandrum* (*P. emodi*). It contains not less than 50% of total aryltetralin lignans, calculated as podophyllotoxin.

An amorphous powder, varying in colour from light brown to greenish-yellow or brownish-grey masses, with a characteristic odour; caustic. On exposure to light or to temperatures above 25° it becomes darker in colour.

Partly soluble in hot water but precipitated again on cooling; partly soluble in chloroform, in ether, and in dilute ammonia solution. Protect from light.

USP 31 (Podophyllum Resin). The powdered mixture of resins extracted from podophyllum (the rhizomes and roots of *Podophyllum peltatum*) by percolation with alcohol and subsequent precipitation with acidified water. It contains not less than 40% and not more than 50% of hexane-insoluble matter.

An amorphous caustic powder, varying in colour from light brown to greenish-yellow. On exposure to light or to temperatures above 25° it becomes darker in colour.

Soluble in alcohol with a slight opalescence; partially soluble in chloroform and in ether. A solution in alcohol is acid to litmus. Store in airtight containers. Protect from light.

Podophyllotoxin *(BAN)*

Podofilotoxina; Podofilox *(USAN)*; Podofyllotoksiini; Podofyllotoxin; Podophyllotoxinum. (5*R*,5a*R*,8a*R*,9*R*)-5,5a,6,8,8a,9-Hexahydro-9-hydroxy-5-(3,4,5-trimethoxyphenyl)furo[3′4′:6,7]naphtho[2,3-*d*]-1,3-dioxol-6-one.

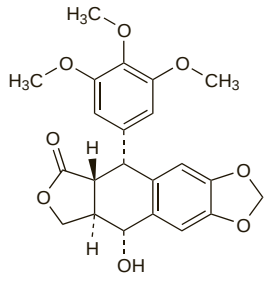
Подофиллотоксин

$C_{22}H_{22}O_8$ = 414.4.

CAS — 518-28-5.

ATC — D06BB04.

ATC Vet — QD06BB04.



Adverse Effects

Podophyllum is very irritant, especially to the eyes and mucous membranes. It can also cause severe systemic toxicity after ingestion or topical application, which is usually reversible but has been fatal. Symptoms of toxicity include nausea, vomiting, abdominal pain, and diarrhoea; there may be thrombocytopenia, leucopenia, renal failure, and hepatotoxicity. Central effects are delayed in onset and prolonged in duration and include acute psychotic reactions, hallucinations, confusion, dizziness, stupor, ataxia, hypotonia, seizures, and coma. EEG changes may persist for several days. Peripheral and autonomic neuropathies develop later and may result in paraesthesias, reduced reflexes, muscle weakness, tachycardia, apnoea, orthostatic hypotension, paralytic ileus, and urinary retention. Neuropathy may persist for several months.

Poisoning. Reports and reviews of podophyllum toxicity.[1-7] A few of the cases followed consumption of herbal preparations containing podophyllum or the related plant bajiaolian (*Dysosma pleianthum*). Death has occurred after ingestion of 10 g of podophyllum.

1. Cassidy DE, *et al.* Podophyllum toxicity: a report of a fatal case and a review of the literature. *J Toxicol Clin Toxicol* 1982; **19:** 35–44.
2. Dobb GJ, Edis RH. Coma and neuropathy after ingestion of herbal laxative containing podophyllin. *Med J Aust* 1984; **140:** 495–6.
3. Holdright DR, Jahangiri M. Accidental poisoning with podophyllin. *Hum Exp Toxicol* 1990; **9:** 55–6.
4. Tomczak RL, Hake DH. Near fatal systemic toxicity from local injection of podophyllin for pedal verrucae treatment. *J Foot Surg* 1992; **31:** 36–42.
5. Kao W-F, *et al.* Podophyllotoxin intoxication: toxic effect of bajiaolian in herbal therapeutics. *Hum Exp Toxicol* 1992; **11:** 480–7.
6. Chan TYK, Critchley JAJH. Usage and adverse effects of Chinese herbal medicines. *Hum Exp Toxicol* 1996; **15:** 5–12.
7. Chu CC, *et al.* Sensory neuropathy due to bajiaolian (podophyllotoxin) intoxication. *Eur Neurol* 2000; **44:** 121–3.

Precautions

The risk of systemic toxicity after topical application of podophyllum is increased by the treatment of large areas with excessive amounts for prolonged periods, by the treatment of friable, bleeding, or recently biopsied warts, and by inadvertent application to normal skin or mucous membranes.

Podophyllum should not be used during pregnancy or breast feeding. There are few reports of use during pregnancy and a teratogenic risk cannot be ruled out. Adverse systemic effects in the mother would also be undesirable during pregnancy, and there are other non-drug treatments available for the treatment of anogenital warts. It is not known whether podophyllum is distributed into breast milk.

Handling. Podophyllum resin is strongly irritant to the skin, eyes, and mucous membranes and requires careful handling.

Uses and Administration

Podophyllum resin and podophyllotoxin have an antimitotic action and are used principally as topical treatments for anogenital warts (condylomata acuminata). Podophyllum resin and podophyllotoxin may be used on external genital and perianal warts; podophyllum resin may also be used on urethral meatus warts. However, neither of these compounds should be used to treat warts on mucous membranes, including vaginal, cervical, intra-urethral, intra-anal, and rectal warts.

Podophyllum resin is usually formulated in compound benzoin tincture in strengths of 15% Indian podophyllum resin or 10 to 25% American podophyllum resin. Lower concentrations of American podophyllum resin in alcoholic solutions have been used. The solution is left on the warts for 1 to 6 hours, and then washed off. Only a small area or number of warts should be treated at any one time and care must be taken to avoid application to healthy tissue. This procedure is carried out once a week for up to 3 to 6 weeks. Preparations containing podophyllotoxin 0.5% in alcohol or alcoholic gel or podophyllotoxin 0.15% cream are used similarly. They are applied twice daily for 3 days but not washed off. Treatment may be repeated at weekly intervals for up to a total of 4 or 5 weeks of treatment. Podophyllum resin is also used with other keratolytics for the removal of plantar warts.

Although podophyllum resin and podophyllotoxin preparations are generally not used in children, see below.

When taken orally podophyllum resin is highly irritant to the intestinal mucosa and produces violent peristalsis resulting in a drastic purging action. It has been superseded by less toxic laxatives.

Podophyllum has been used in homoeopathic medicine.

Administration in children. The use of podophyllum resin and podophyllotoxin preparations in children is generally avoided because of the potential for severe local irritation and systemic toxicity. Nonetheless, podophyllotoxin has been used for the