6. Pericin M, Trüeb RM. Topical immunotherapy of severe alopecia areata with diphenylcyclopropenone: evaluation of 68 cases. *Dermatology* 1998; **196:** 418–21.
7. Cotellessa C, *et al.* The use of topical diphenylcyclopropenone for the treatment of extensive alopecia areata. *J Am Acad Dermatol* 2001; **44:** 73–6.
8. Wiseman MC, *et al.* Predictive model for immunotherapy of alopecia areata with diphencyprone. *Arch Dermatol* 2001; **137:** 1063–8.
9. van der Steen PHM, *et al.* Topical immunotherapy for alopecia areata: re-evaluation of 139 cases after an additional follow-up period of 19 months. *Dermatology* 1992; **184:** 198–201.

Warts. Diphencyprone has been tried in the treatment of recalcitrant warts. The successful treatment of digital or plantar warts in 42 of 60 patients has been described.[1] The patients were initially sensitised with a 2% topical solution of diphencyprone in acetone, then the warts treated every 1 to 4 weeks with solutions ranging from 0.01 to 6%. In another series,[2] diphencyprone in a paraffin ointment was effective in the clearance of palmar, plantar, palmoplantar, and periungual warts in 135 of 154 patients. A concentration of diphencyprone 2% was used for the initial sensitisation, and concentrations of 0.5 to 4% were used for treatment once every 3 weeks. After initial sensitisation with diphencyprone 2% in acetone, a preparation of diphencyprone with salicylic acid in white soft paraffin applied every night as tolerated was reported to be successful in 44 of 50 patients treated for palmoplantar warts.[3] The concentration of diphencyprone in the ointment ranged from 0.01 to 0.2%, and the concentration of salicylic acid was 15%.

1. Buckley DA, *et al.* Recalcitrant viral warts treated by diphencyprone immunotherapy. *Br J Dermatol* 1999; **141:** 292–6.
2. Upitis JA, Krol A. The use of diphenylcyclopropenone in the treatment of recalcitrant warts. *J Cutan Med Surg* 2002; **6:** 214–17.
3. Armour K, Orchard D. Treatment of palmoplantar warts with a diphencyprone and salicylic acid ointment. *Australas J Dermatol* 2006; **47:** 182–5.

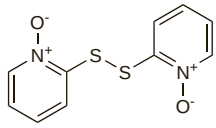
Dipyrithione *(USAN, rINN)*

Bispiriyon; Bispyrithione; Dipiritiona; Dipyrithionum; OMDS; Piriyon Disülfit; Pyrithione Disulfide. 2,2′-Dithiodipyridine 1,1′-dioxide.

Дипиритион

$C_{10}H_8N_2O_2S_2$ = 252.3.

CAS — 3696-28-4.



Profile

Dipyrithione is reported to have antibacterial and antifungal properties and is included in preparations for the treatment of dandruff.

Preparations

Proprietary Preparations (details are given in Part 3)

Turk.: Perkapil.

Multi-ingredient: ***Canad.:*** Dan-Tar Plus; Polytar AF; ***Switz.:*** Crimanex.

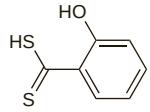
Dithiosalicylic Acid

Ditiosalicílico, ácido. 2-Hydroxybenzenecarbodithioic acid.

Дитиосалициловая Кислота

$C_7H_6OS_2$ = 170.3.

CAS — 527-89-9.



Profile

Dithiosalicylic acid has been used in multi-ingredient preparations used topically for the treatment of acne and seborrhoeic dermatitis.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Ital.:*** Sacnel.

Dithranol *(BAN, rINN)*

Anthralin; Antralin; Dioxyanthranol; Dithranolum; Ditranol; Ditranoli; Ditranolis. 1,8-Dihydroxyanthrone; 1,8-Dihydroxy-9(10*H*)-anthracenone.

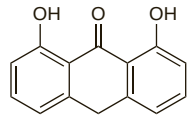
Дитранол

$C_{14}H_{10}O_3$ = 226.2.

CAS — 1143-38-0 (dithranol); 16203-97-7 (dithranol triacetate).

ATC — D05AC01.

ATC Vet — QD05AC01.



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

Ph. Eur. 6.2 (Dithranol). A yellow or brownish-yellow, crystalline powder. Practically insoluble in water; slightly soluble in alcohol; sparingly soluble in acetone; soluble in dichloromethane; dissolves in dilute solutions of alkali hydroxides. Protect from light.

USP 31 (Anthralin). A yellowish-brown, odourless, crystalline powder. Insoluble in water; slightly soluble in alcohol, in ether, and in glacial acetic acid; soluble in acetone, in chloroform, in benzene, and in solutions of alkali hydroxides. The filtrate from a suspension in water is neutral to litmus. Store at a temperature of 8° to 15° in airtight containers. Protect from light.

Stability. The stability of dithranol has been studied in a number of bases and vehicles.[1-4] The weaker preparations of dithranol may be less stable.[1,3,4] Salicylic acid is included in dithranol preparations as an antoxidant and its inclusion in pastes also containing zinc oxide prevents their discoloration due to the inactivation of dithranol by zinc oxide.[5] However, zinc oxide or starch can be omitted from dithranol pastes without loss of effectiveness provided stiffness is maintained.[5] Addition of ascorbic or oxalic acid may improve dithranol's stability in '*Unguentum Merck*' but salicylic acid appears to be ineffective.[1] The effect of salicylic acid on the instability of dithranol in yellow soft paraffin is variable[1,2] and its inclusion has been questioned as it can be irritant and percutaneous absorption can be significant.[1] Dithranol is relatively stable in white soft paraffin.[1]

The application of any type of heat and contact with metal spatulas should be avoided during the manufacture of dithranol pastes[6] and if milling facilities are not available dithranol can be incorporated into Lassar's paste by dissolving it first in chloroform.[5]

1. Green PG, *et al.* The stability of dithranol in various bases. *Br J Dermatol* 1985; **113** (suppl 29): 26.
2. Lee RLH. Stability of dithranol (anthralin) in various vehicles. *Aust J Hosp Pharm* 1987; **17:** 254–8.
3. Hiller C, *et al.* How stable is dithranol? An investigation into the degradation of different dithranol formulations. *Pharm Pract* 1995; **5:** 428–31.
4. Thoma K, Holzmann C. Stabilization of dithranol in topical formulations. *Acta Pharm Hung* 1998; **68:** 313–21.
5. Comaish S, *et al.* Factors affecting the clearance of psoriasis with dithranol (anthralin). *Br J Dermatol* 1971; **84:** 282–9.
6. *PSGB Lab Report P/79/1* 1979.

Adverse Effects and Precautions

Dithranol may cause a burning sensation especially on perilesional skin. Patients with fair skin may be more sensitive than those with dark skin. It is irritant to the eyes and mucous membranes. Use on the face, skin flexures, and genitals should be avoided. Hands should be washed after use.

Dithranol should not be used for acute or pustular psoriasis or on inflamed skin. It stains skin, hair, some fabrics, plastics, and enamel. Staining of bathroom ware may be less of a problem with creams than ointments. Stains on skin and hair slowly disappear on cessation of treatment.

Handling. Dithranol is a powerful irritant and should be kept away from the eyes and tender parts of the skin.

Uses and Administration

Dithranol is used in the treatment of subacute and chronic psoriasis, usually in one of two ways.

Conventional treatment is commonly started with an ointment or paste containing 0.1% dithranol (0.05% in very fair patients) applied for a few hours; the strength is gradually increased as necessary to 0.5%, occasionally to 1%, and the duration of contact extended to overnight periods or longer. The preparation is sparingly and accurately applied to the lesions only. If, on initial treatment, lesions spread or excessive irritation occurs, the concentration of dithranol or the frequency of application should be reduced; if necessary, treatment should be stopped. After each treatment period the patient should bathe or shower to remove any residual dithranol.

For *short-contact therapy* dithranol is usually applied in a soft basis to the lesions for up to 60 minutes daily, before being washed off. As with conventional treatment the strength used is gradually increased from 0.1 to 2% but strengths up to 5% have been used. Surrounding unaffected skin may be protected by white soft paraffin.

Treatment for psoriasis should be continued until the skin is entirely clear. Intermittent courses may be needed to maintain the response. Treatment schedules often involve coal tar and UV irradiation (preferably UVB) before the application of dithranol (see below). Salicylic acid is included in many topical preparations of dithranol.

A cream containing dithranol triacetate has been used similarly to dithranol in conventional treatment of psoriasis.

Alopecia. Dithranol cream (0.5 to 1%) applied for 20 to 60 minutes to the scalp and then washed off, has been found to be of benefit in the treatment of alopecia areata (p.1577). However, at least 6 months of treatment may be required for a cosmetically acceptable result.[1] The response rate has, however, been difficult to evaluate because of the small number of reports, and although it has been widely prescribed for limited patchy alopecia areata, some guidelines conclude that there is no convincing evidence of efficacy.[2]

1. Meidan VM, Touitou E. Treatments for androgenetic alopecia and alopecia areata: current options and future prospects. *Drugs* 2001; **61:** 53–69.
2. MacDonald Hull SP, *et al.* British Association of Dermatologists. Guidelines for the management of alopecia areata. *Br J Dermatol* 2003; **149:** 692–9. Also available at: http://www.bad.org.uk/healthcare/guidelines/Alopecia_Areata.pdf (accessed 27/09/07)

Psoriasis. Dithranol used alone or with coal tar, (with or without ultraviolet light), continues to be one of the drugs of first-line treatment for psoriasis (p.1583). It is particularly suited to the treatment of stable chronic plaque psoriasis but unlike coal tar, is irritant to healthy skin and care is required to ensure that it is only applied to lesions. Treatment with dithranol is therefore more feasible when the plaques are large, or few in number. Use with coal tar may help to reduce the irritant effects of dithranol without affecting efficacy. Traditional treatment with dithranol is time consuming and more suitable for use on hospital inpatients. Dithranol formulated in stiff preparations such as Lassar's paste to minimise spreading to perilesional skin is left on overnight covered with a suitable dressing and washed off the next day. Treatment is usually started with a concentration of 0.1% (0.05% in fair-skinned patients) and gradually increased according to the response and irritation produced. Cream formulations may be less effective but are more suitable for domestic use. Short-contact therapy in which concentrations of up to 5% of dithranol are applied daily for up to 1 hour is more suitable for use on an outpatient basis and there appears to be little reduction in efficacy; irritation and staining may also be reduced.

Dithranol is also used with UVB phototherapy and there have been many modifications of the original Ingram's regimen in which dithranol is applied after bathing in a tar bath and exposure to ultraviolet light. Inpatient stays of up to 3 weeks may be required but long periods of remission can be obtained.

Reviews.

1. Mahrle G. Dithranol. *Clin Dermatol* 1997; **15:** 723–37.

Preparations

BP 2008: Dithranol Cream; Dithranol Ointment; Dithranol Paste;
USP 31: Anthralin Cream; Anthralin Ointment.

Proprietary Preparations (details are given in Part 3)

Austral.: Dithrocream†; Micanol†; ***Austria:*** Micanol; ***Belg.:*** Micanol†; ***Canad.:*** Anthraforte; Anthranol; Anthrascalp; Micanol†; ***Denm.:*** Micanol†; ***Fin.:*** Micanol†; ***Ger.:*** Micanol; ***Hong Kong:*** Micanol†; ***India:*** Psorinol; ***Indon.:*** Anthramed; ***Irl.:*** Dithrocream; Micanol†; ***Israel:*** Dithrocream; Micanol; ***Ital.:*** Psoriderm; Timicolid†; ***Neth.:*** Psoricreme; Psoristick; ***Norw.:*** Micanol; ***NZ:*** Micanol; ***Port.:*** Micanol; ***S.Afr.:*** Anthranol; ***Spain:*** Micanol; ***Swed.:*** Micanol; ***Thai.:*** Micanol†; ***UK:*** Dithrocream; Micanol; ***USA:*** Anthra-Derm†; Dritho-Scalp; Drithocreme†; Psoriatec.

Multi-ingredient: ***Austral.:*** Dithrasal; ***Fr.:*** Anaxeryl; ***Ger.:*** Psoradexan; Psoralon MT; ***Hong Kong:*** Dithrasal; ***India:*** Derobin Skin; ***Singapore:*** Dithrasal; ***Spain:*** Lapices Epiderm Metadier; ***Turk.:*** Psoraks; ***UK:*** Psorin.