

tion,^{3,10} gastrointestinal effects,^{2,4,10,11} and flushing.^{2,4,10,11} There has been a report of exanthema in a patient receiving dimethyl fumarate for lichen planus.¹²

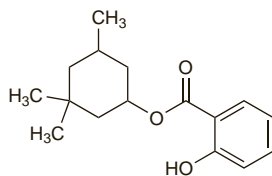
- van Loenen AC, *et al.* Fumaarzuurtherapie: van fictie tot werkelijkheid? *Pharm Weekbl* 1989; **124**: 894-900.
- Kolbach DN, Nieboer C. Fumaric acid therapy in psoriasis: a long-term retrospective study on the effect of fumaric acid combination (FAC-EC) therapy and dimethyl-fumaric acid ester (DMFAE) monotherapy. *Br J Dermatol* 1990; **123**: 534-5.
- Nugteren-Huying WM, *et al.* Fumaric acid therapy for psoriasis: a randomized, double-blind, placebo-controlled study. *J Am Acad Dermatol* 1990; **22**: 311-12.
- Altmeyer PJ, *et al.* Antipsoriatic effect of fumaric acid derivatives: results of a multicenter double-blind study in 100 patients. *J Am Acad Dermatol* 1994; **30**: 977-81.
- Mrowietz U, *et al.* Treatment of severe psoriasis with fumaric acid esters: scientific background and guidelines for therapeutic use. *Br J Dermatol* 1999; **141**: 424-9.
- Ständer H, *et al.* Efficacy of fumaric acid ester monotherapy in psoriasis pustulosa palmoplantaris. *Br J Dermatol* 2003; **149**: 220-2.
- Anonymous. Fumaric acid derivatives and nephrotoxicity. *WHO Drug Inf* 1990; **4**: 28.
- Hoefnagel JJ, *et al.* Long-term safety aspects of systemic therapy with fumaric acid esters in severe psoriasis. *Br J Dermatol* 2003; **149**: 363-9.
- Harries MJ, *et al.* Fumaric acid esters for severe psoriasis: a retrospective review of 58 cases. *Br J Dermatol* 2005; **153**: 549-51.
- Nieboer C, *et al.* Systemic therapy with fumaric acid derivatives: new possibilities in the treatment of psoriasis. *J Am Acad Dermatol* 1989; **20**: 601-8.
- Mrowietz U, *et al.* Treatment of psoriasis with fumaric acid esters: results of a prospective multicentre study. *Br J Dermatol* 1998; **138**: 456-60.
- Guenther CH, *et al.* Macular exanthema due to fumaric acid esters. *Ann Pharmacother* 2003; **37**: 234-6.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Ingepsor; **Ger.**: Psoriasis-Solution†; Psoriasis-Tabletten†

Multi-ingredient Arg.: Noquerat†; **Austral.**: Pro-PS†; **Ger.**: Fumaderm; Psoriasis-Bad†; Psoriasis-Salbe †;



NOTE. Eusolex HMS and Neo-Heliopan HMS are trade names that have been used for homosalate.

Pharmacopoeias. In US.

USP 31 (Homosalate). Store in airtight containers.

Profile

Homosalate, a substituted salicylate, is a sunscreen (p.1576) with actions similar to those of octisalate (p.1608). It is effective against UVB light (for definitions, see p.1580).

Preparations

Proprietary Preparations numerous preparations are listed in Part 3.

Hydroquinone

Hidrokinon; Hidrokinona; Hydrochinon; Hydrochinonum; Quinol. 1,4-Benzenediol.

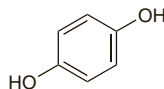
Гидрохинон

$C_6H_6O_2 = 110.1$.

CAS — 123-31-9.

ATC — D11AX11.

ATC Vet — QD11AX11.



NOTE. Do not confuse with Hydroquinine (p.2322).

Pharmacopoeias. In US.

USP 31 (Hydroquinone). Fine white needles which darken on exposure to light and air. Soluble 1 in 17 of water, 1 in 4 of alcohol, 1 in 51 of chloroform, and 1 in 16.5 of ether. Store in airtight containers. Protect from light.

Adverse Effects, Treatment, and Precautions

Topical hydroquinone may cause transient erythema and a mild burning sensation. Occasionally hypersensitivity has occurred and US licensed product information recommends skin testing before use. Hydroquinone should not be applied to abraded or sunburnt skin. It should not be used to bleach eyelashes or eyebrows and contact with the eyes should be avoided as it may produce staining and corneal opacities. High concentrations or prolonged use may produce a blue-black hyperpigmentation (ochronosis) or pigmented colloid milium. The systemic effects of hydroquinone and their treatment are similar to those of phenol (see p.1656) but tremors and convulsions may also occur.

Carcinogenicity. There is some evidence from *animal* studies that hydroquinone might be carcinogenic (see Effects on the Skin, below).

Effects on the liver. Toxic hepatitis in a radiographer was attributed to occupational exposure to hydroquinone fumes from the developing medium used in the darkroom.¹ However, it has been pointed out² that hydroquinone is not volatile under normal conditions of use and that surveillance of 879 people engaged in the manufacture and use of hydroquinone from 1942 to 1990 found no association between toxic hepatitis and hydroquinone exposure.

- Nowak AK, *et al.* Darkroom hepatitis after exposure to hydroquinone. *Lancet* 1995; **345**: 1187.
- O'Donoghue JL, *et al.* Hydroquinone and hepatitis. *Lancet* 1995; **346**: 1427-8.

Effects on the skin. The incidence of exogenous ochronosis (blue-black hyperpigmentation) in a survey of black South African patients was found to be 15% in males and 42% in females with 69% of affected individuals admitting to using hydroquinone-containing preparations.¹ This was considered to be more consistent with a toxic effect of a drug with a low therapeutic index, rather than an idiosyncratic reaction. The data revealed that even preparations with hydroquinone 2% or less with a sun-

screen produced ochronosis. Ochronosis usually became apparent after about 6 months of use and, once established, was probably irreversible. Patients may initially use skin lighteners for cosmetic purposes but once ochronosis develops they may fall into the 'skin lightener trap' as they use other hydroquinone preparations to remove the disfigurement.¹ Treatment of exogenous ochronosis is based on stopping the use of hydroquinone, but it may take years for any improvement to be apparent. There are a few reports of benefit from topical tretinoin, dermabrasion, and laser therapy, but these are far from established therapies.² Reversible brown discoloration of the nails has also been reported after the use of skin lighteners containing hydroquinone.³⁻⁵

In addition to the risk of ochronosis it has been suggested that, based on *animal* studies, long-term use of hydroquinone might be carcinogenic.⁶ In the USA, preparations containing up to 2% hydroquinone may be sold without prescription, but in 2006, based on data regarding potential carcinogenicity and reports of ochronosis, the FDA proposed to reclassify these products as drugs and make them available by prescription only.⁷ In Europe the use of hydroquinone in cosmetic preparations for skin lightening is already banned, but it is still available for prescription as a medicine.⁶

- Hardwick N, *et al.* Exogenous ochronosis: an epidemiological study. *Br J Dermatol* 1989; **120**: 229-38.
- Levin CY, Maibach H. Exogenous ochronosis: an update on clinical features, causative agents and treatment options. *Am J Clin Dermatol* 2001; **2**: 213-17.
- Mann RJ, Harman RRM. Nail staining due to hydroquinone skin-lightening creams. *Br J Dermatol* 1983; **108**: 363-5.
- Ozluer SM, Muir J. Nail staining from hydroquinone cream. *Australas J Dermatol* 2000; **41**: 255-6.
- Parlak AH, *et al.* Discolouration of the fingernails from using hydroquinone skin-lightening cream. *J Cosmet Dermatol* 2003; **2**: 199-201.
- Kooyers TJ, Westerhof W. Toxicology and health risks of hydroquinone in skin lightening formulations. *J Eur Acad Dermatol Venereol* 2006; **20**: 777-80.
- FDA. Skin bleaching drug products for over-the-counter human use: proposed rule. *Fed Regist* 2006; **71**: 51146-55. Available at: <http://a257.g.akamaitech.net/7/257/2422/01jan20061800/edocket.access.gpo.gov/2006/pdf/E6-14263.pdf> (accessed 27/09/07)

Uses and Administration

Hydroquinone increases melanin excretion from melanocytes and may also prevent its production. Hydroquinone is used topically as a depigmenting agent for the skin in hyperpigmentation conditions (p.1582) such as chloasma (melasma), freckles, and lentigines (liver spots). Concentrations of 2 to 4% are commonly used; higher concentrations may be very irritant and increase the risk of ochronosis. It may be several weeks before any effect is apparent but depigmentation may last for 2 to 6 months after stopping. Application of hydroquinone should stop if there is no improvement after 2 months. Hydroquinone should be applied twice daily only to intact skin which should be protected from sunlight to reduce repigmentation. A preparation containing hydroquinone 4%, tretinoin 0.05%, and fluciclonolone acetone 0.01% may be applied once daily at night in the treatment of chloasma (melasma). Hydroquinone preparations often include a sunscreen or a sunblocking basis.

Hydroquinone is also used as an antioxidant in topical preparations and in photographic developers.

Preparations

USP 31: Hydroquinone Cream; Hydroquinone Topical Solution.

Proprietary Preparations (details are given in Part 3)

Arg.: Claripel; **Braz.**: Claripel; **Solauquin Canad.**: African Gold†; Banishing Cream; Eldopaque; Eldoquin; Esoterica Regular; Esoterica Unscented; Lustra; Nadinola†; NeoStrata Canada HQ Plus; Porcelana Nighttime Formula†; Ultraquin Plain; **Chile:** Etnoderm; Unitone 4; **Hong Kong:** Derma-Rx Lightener; Eldopaque; Eldoquin; Solauquin; **Indon.**: Bioquin; Mediquin; Melanox; Melaskin; Pigmet; Pylauquin; Qutifair; **Israel:** Esomed; **Malaysia:** Eldopaque; Eldoquin; **Mex.**: Crema Blanca; Eldopaque; Eldoquin; Hidroquin; Melanex; Quinoret Forte; **NZ:** Eldoquin; **Singapore:** Eldopaque; Eldoquin; Polyquin; **Solauquin Spain:** Hidroquillaud; Licostrata; Melanasa; Nadona; Pigmentasa; **Thail.**: Clariderm; **Turk.**: Expigmet; **UK:** Eldopaque; Eldoquin; Solauquin; **USA:** Actlaro; Claripel; Eldopaque; Eldoquin; EpiQuin; Esoterica Regular; Lustra; Solauquin; **Venez.**: Pharquinor†;

Multi-ingredient Arg.: Melaclear†; Melasmax; Neocuticals Crema Despigmentante de Dia†; Neocuin; Neocuin Forte; Neostara Gel Despigmentante; Solauquin Forte; Tri-Luma; **Austral.**: Superfade; **Braz.**: Glyquin; Tri-Luma; Vitacid Plus; **Canad.**: Esoterica; Glyquin XM†; Lustra-AF; NeoStrata Canada HQ Plus; NeoStrata HQ; Porcelana Daytime Formula†; Solauquin Forte†; Ultraquin; Viquin Forte†; **Chile:** Alastik†; Clasifel; D 4†; Neostara; Tri-Luma; Trio-D†; **Ger.**: Pigmanorm; **Hong Kong:** Glyquin; Superfade; Tri-Luma; **India:** Melalite 15; **Indon.**: Hidrogel; Interquin; Interquin Plus; NeoDerm Sunblock; **Malaysia:** Solauquin Forte; Tri-Luma; **Mex.**: Clasifel; Nova Derm; Quinoret; Solauquin; Tri-Luma; **Philipp.**: Tri-Luma; **Singapore:** Glyquin; Glyquin XM†; Tri-Luma; **Switz.**: Pigmanorm; **Thail.**: Tri-Luma; **Turk.**: Metamorfoz; **USA:** Esoterica Facial and Sunscreen; Glyquin XM†; Solauquin Forte; Tri-Luma; **Venez.**: Tri-Luma.

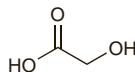
Glycolic Acid

Glicólico, ácido; Hydroxyacetic Acid. Hydroxyethanoic acid.

Гидроксиуксусная Кислота; Гликолевая Кислота

$C_2H_4O_3 = 76.05$.

CAS — 79-14-1.



Profile

Glycolic acid is an alpha hydroxy organic acid that has been used in topical preparations for hyperpigmentation (see Pigmentation Disorders, p.1582) and photodamaged skin (see Photoaging, p.1581).

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Alfabase 8; Gelofort†; Glicoidin; Gligel; Lactrime†; Lipomax†; Loxidi†; Vansame G; **Canad.**: Reversa; **Chile:** Alastik†; Neosolets; Teen Derm†; **Hong Kong:** Glyderm; **Indon.**: Exfoliac; Glycare; **Ital.**: Neostrata; Revitalizing†; **Malaysia:** Glyderm†; **Mex.**: Glicoderm; Glicolic; Nova Derm; **Philipp.**: Teranex; **Singapore:** Glyderm; Sensesense Anti-Ageing; **Venez.**: Glyco-A†; Teen Derm†;

Multi-ingredient Arg.: Celskinlab C + AHA; Controlacne; Diacneal; Efficacy; Hidroskin; Hydragen†; Keracnyl; Melaclear†; Negacne; Neocuin; Neocuin Forte; Neostrata; Neostrata Gel Despigmentante; Purasoft; Revital; Vansame GS; Vansame Plus; **Austral.**: Neostrata; **Braz.**: Glyquin; **Canad.**: Biobase-G; Dilusol/AHA†; Glyquin XM†; Neostrata; NeoStrata Blemish Spot Gel; NeoStrata Daytime; NeoStrata HQ; Reversa UV; Viquin Forte†; **Chile:** Alastik†; D 4†; Diacneal; Neostrata; Neutrogena Healthy Skin; Neutrogena Limpidiora; Primacy C+AHA†; Ureadin Forte; **Fr.**: Alpha S DS†; Aniospar 29; Body Peel; Cleanance K; Correcteur Anti-Taches; Cosmodex Uniwwhite†; Day Peel; Hyfac soin keratolytique†; Item Alphapeptol; Kelual DS; Keracnyl; Keracnyl eau nettoyante; Keracnyl stop bouton; Kertyol-S; Night Peel; Photakne†; Seborheane; **Hong Kong:** Glyquin; **Indon.**: Exfoliac; Interquin Plus; **Ital.**: Acnesani†; Biophase Shampoo; Lightening; Neocuticals Spot Treatment; Phytic Acid; Same-Seb Beta; Sebacnol†; **Mex.**: Nova Derm; **Port.**: Bioclin Sebo Care; Ureadin; Ureadin Forte; **Singapore:** Glyquin; Glyquin XM†; Percutalfa; **USA:**: Glyquin XM†; **Venez.**: Diacneal; Photoderm AKN.

Homosalate (USAN, *INN*)

Homomenthyl Salicylate; Homosalato; Homosalatum. 3,3,5-Tri-methylcyclohexyl salicylate.

Гомосалат

$C_{16}H_{22}O_3 = 262.3$.

CAS — 118-56-9.