

liquid. Very slightly soluble in water; miscible with alcohol, and with fatty and essential oils. Protect from light.

USNF 26 (Methyl Salicylate). It is produced synthetically or is obtained from the leaves of *Gaultheria procumbens* (Ericaceae) [wintergreen] or from the bark of *Betula lenta* (Betulaceae) [sweet or black birch]. The source of the methyl salicylate must be indicated on the label.

A colourless, yellowish, or reddish liquid having the characteristic odour of wintergreen. Slightly soluble in water; soluble in alcohol and in glacial acetic acid. Store in airtight containers.

Storage. Certain plastic containers, such as those made from polystyrene, are unsuitable for liniments or ointments containing methyl salicylate.

Adverse Effects, Treatment, and Precautions

Salicylate intoxication can occur after ingestion or topical application of methyl salicylate (see Overdosage, below).

Overdosage. Ingestion of methyl salicylate poses the threat of severe, rapid-onset salicylate poisoning because of its liquid concentrated form and lipid solubility.¹ It is readily absorbed from the gastrointestinal tract and most is rapidly hydrolysed to free salicylate. The symptoms, which may appear within 2 hours of ingestion, are similar to those of salicylate poisoning in general (see Adverse Effects of Aspirin, p.20), although methyl salicylate is expected to be more toxic because of its lipid solubility. There have been reports of fatalities after ingestion of as little as 4 mL in a child and 6 mL in an adult, although the adult lethal dose is estimated to be 30 mL.¹ Topical Chinese herbal medicinal preparations may contain methyl salicylate in variable amounts, and salicylate poisoning has been reported in a 40-year-old man after a total body application of such a preparation.² Salicylate poisoning has also been reported in a woman who had attempted suicide by ingesting Red Flower Oil, a topical Chinese herbal oil.³ The authors also noted that some patients took small amounts of this preparation orally in an attempt to enhance its analgesic effects.

- Chan TYK. Potential dangers from topical preparations containing methyl salicylate. *Hum Exp Toxicol* 1996; **15**: 747–50.
- Bell AJ, Duggin G. Acute methyl salicylate toxicity complicating herbal skin treatment for psoriasis. *Emerg Med (Fremantle)* 2002; **14**: 188–90.
- Chan TH, et al. Severe salicylate poisoning associated with the intake of Chinese medicinal oil ('Red Flower Oil'). *Aust N Z J Med* 1995; **25**: 57.

Percutaneous absorption. Like other salicylates, methyl salicylate may be absorbed through intact skin.¹ Percutaneous absorption is enhanced by exercise, heat, occlusion, or disruption of the integrity of the skin. The amount absorbed will also be increased by application to large areas of skin.

Results from a study in healthy subjects showed that a considerable amount of salicylic acid may be absorbed through the skin after topical application of products containing methyl salicylate.² Both the rate and extent of absorption increased after repeated application; the bioavailability of the ointment preparation used in the study increased from 15% after the second dose to 22% after the third to eighth dose. The authors recommend that topical analgesic preparations containing methyl salicylate or other salicylates should be used with caution in patients at increased risk of developing salicylate adverse effects (see Precautions of Aspirin, p.22).

Results from another study³ showing high tissue to plasma ratios after topical application of a methyl salicylate formulation suggest that direct penetration and not recirculation in the blood is responsible for the salicylate concentrations found. The results also showed that methyl salicylate is extensively metabolised to salicylic acid in the dermal and subcutaneous tissues after topical application.

However, for a study suggesting limited absorption from a patch preparation containing camphor, menthol, and methyl salicylate, see Menthol, p.2340.

- Chan TYK. Potential dangers from topical preparations containing methyl salicylate. *Hum Exp Toxicol* 1996; **15**: 747–50.
- Morra P, et al. Serum concentrations of salicylic acid following topical applied salicylate derivatives. *Ann Pharmacother* 1996; **30**: 935–40.
- Cross SE, et al. Is there tissue penetration after application of topical salicylate formulations? *Lancet* 1997; **350**: 636.

Interactions

Absorption of methyl salicylate through the skin can occur after excessive topical application (see above), and interactions would be expected to be as for other salicylates (see Interactions of Aspirin, p.23).

Anticoagulants. Potentiation of warfarin anticoagulation has been reported¹⁻³ after topical application of methyl salicylate preparations.

- Littleton F. Warfarin and topical salicylates. *JAMA* 1990; **263**: 2888.
- Tam LS, et al. Warfarin interactions with Chinese traditional medicines: danshen and methyl salicylate medicated oil. *Aust N Z J Med* 1995; **25**: 258.
- Joss JD, LeBlond RF. Potentiation of warfarin anticoagulation associated with topical methyl salicylate. *Ann Pharmacother* 2000; **34**: 729–33.

Uses and Administration

Methyl salicylate is a salicylic acid derivative that is irritant to the skin and is used topically in rubefacient preparations for the relief

of pain in musculoskeletal, joint, and soft-tissue disorders. It is also used for minor peripheral vascular disorders such as chilblains and as an ingredient in inhalations for the symptomatic relief of upper respiratory-tract disorders.

Wintergreen oil is also used in aromatherapy.

Preparations

BP 2008: Kaolin Poultice; Methyl Salicylate Liniment; Methyl Salicylate Ointment; Surgical Spirit.

Proprietary Preparations (details are given in Part 3)

Arg.: Aspi-Rub†; Rati Salil Gel; **Austral.:** Linsal†; **Canad.:** Deep Heating; **Chile:** Parche Calorub; **Ger.:** Hewedolor N; **India:** Dolocide Plus; **Mex.:** Balsamo Nordin; Friction Don Juan; Tolari; **S.Afr.:** Thermo-Rub; **Thai.:** Mygesal; **UK:** Numark Muscle Rub; **USA:** Argesic†; Exocaine†; Gordogesic; **Venez.:** Novofric†; Ultrafril†.

Multi-ingredient: numerous preparations are listed in Part 3.

Mofebutazone (rINN)

Mofebutatoni; Mofebutazon; Mofebutazona; Mofebutazono; Mofebutazonum; Monobutazono; Monophenylbutazono. 4-Butyl-1-phenylpyrazolidine-3,5-dione.

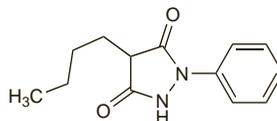
Мофебутазон

$C_{13}H_{16}N_2O_2 = 232.3$.

CAS — 2210-63-1.

ATC — M01AA02; M02AA02.

ATC Vet — QM01AA02; QM02AA02.



Profile

Mofebutazone, a derivative of phenylbutazone (p.117), is an NSAID (p.96). It has been used in the management of musculoskeletal and joint disorders. The sodium salt has been given by intramuscular injection.

Preparations

Proprietary Preparations (details are given in Part 3)

Ger.: Mofesal N†.

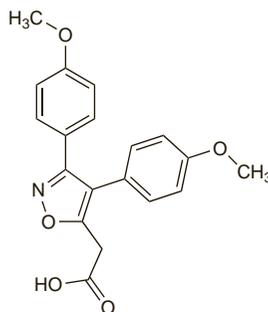
Mofezolac (rINN)

Mofezolac; Mofezolacum; Mofezolacum; N-22, 3,4-Bis(p-methoxyphenyl)-5-isoxazoleacetic acid.

Мофезолак

$C_{19}H_{17}NO_5 = 339.3$.

CAS — 78967-07-4.



Profile

Mofezolac is an NSAID (p.96) given orally in the management of pain and musculoskeletal and joint disorders.

Preparations

Proprietary Preparations (details are given in Part 3)

Jpn.: Disopain.

Morniflumate (USAN, rINN)

Morniflumato; Morniflumatum; UP-164. 2-Morpholinoethyl 2-(α,α -trifluoro-m-toluidino)nicotinate.

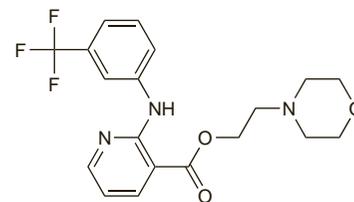
Морнифлумат

$C_{19}H_{20}F_3N_3O_3 = 395.4$.

CAS — 65847-85-0.

ATC — M01AX22.

ATC Vet — QM01AX22.



Profile

Morniflumate, the morpholinoethyl ester of niflumic acid (p.95), is an NSAID (p.96). It has been used in inflammatory conditions in doses of 700 mg given twice daily by mouth or rectally as suppositories.

Preparations

Proprietary Preparations (details are given in Part 3)

Fr.: Nifluril; **Ital.:** Flomax; Flumarin; Morniflu; Niflam; **Spain:** Niflactol.

Morphine (BAN) ⓧ

Morfini; Morfin; Morfina; Morphinum. 7,8-Didehydro-4,5-epoxy-17-methylmorphinan-3,6-diol.

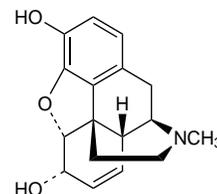
Морфин

$C_{17}H_{19}NO_3 = 285.3$.

CAS — 57-27-2 (anhydrous morphine); 6009-81-0 (morphine monohydrate).

ATC — N02AA01.

ATC Vet — QN02AA01.



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

Adolf; Block; China White; Cube; Dreamer; Drug store dope; Drugstore dope; Emsel; First line; German boy; God's drug; Gomma; Hard stuff; Hospital Heroin; Hows; Hydrogen Bomb; M; Miss Emma; Mister blue; Mojo; Monf; Monkey; Morf; Morfs; Morfa; Morphia; Morphina; Morpho; Morphy; Mr. Blue; M.S.; MS; Mud; Murphy; Nasty; Nazi; Sweet Jesus; Sweet Morpheus; Tar; Unkie; White Stuff.

Morphine Hydrochloride (BANM) ⓧ

Morfinihidrokloridi; Morfin Hidroklorür; Morfina, hidrocloruro de; Morfin-hidroklorid; Morfin-hidrochlorid trihidrát; Morfinhidroklorid; Morfino hidrokloridas; Morfiny chlorowodorek; Morphine, chlorhydrate de; Morphin hydrochloridum; Morphin Hydrochloridum Trihydricum; Morphinii Chloridum; Morphinum Chloratum.

Морфина Гидрохлорид

$C_{17}H_{19}NO_3 \cdot HCl \cdot 3H_2O = 375.8$.

CAS — 52-26-6 (anhydrous morphine hydrochloride); 6055-06-7 (morphine hydrochloride trihydrate).

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn.* and *Viet.* **Ph. Eur. 6.2** (Morphine Hydrochloride). Colourless, silky needles, cubical masses or a white or almost white, crystalline powder. It is efflorescent in a dry atmosphere. Soluble in water; slightly soluble in alcohol; practically insoluble in toluene. Protect from light.

Incompatibility. See under Morphine Sulfate, below.

Morphine Sulfate ⓧ

Morfiniisulfääti; Morfin Sülfat; Morfina, sulfato de; Morfino sulfatas; Morfinsulfat; Morfin-sulfát pentahydrát; Morfin-sulfát; Morfiny siarczan; Morphine, sulfate de; Morphine Sulphate (BANM); Morphinii sulfas; Morphinii Sulfas Pentahydricus.

Морфина Сульфат

$(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4 \cdot 5H_2O = 758.8$.

CAS — 64-31-3 (anhydrous morphine sulfate); 6211-15-0 (morphine sulfate pentahydrate).

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

Ph. Eur. 6.2 (Morphine Sulphate). A white or almost white, crystalline powder. Soluble in water; very slightly soluble in alcohol; practically insoluble in toluene. Protect from light.

USP 31 (Morphine Sulfate). White, feathery, silky crystals, cubical masses of crystals, or a white crystalline powder. Is colourless and when exposed to air it gradually loses water of hy-