

BRITISH  
PHARMACEUTICAL  
CODEX  
1973



PLAINTIFFS'  
TRIAL EXHIBIT  
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# BRITISH PHARMACEUTICAL CODEX 1973



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having a unicellular spherical head. It contains similar alkaloids to those in *H. niger*. Some Indian henbane is derived from *H. reticulatus* L. and contains about 0.12 to 0.24 per cent of alkaloids.

**Storage.** It should be stored in a cool dry place, protected from light.

**Actions and uses.** Hyoscyamus has actions similar to those described under Belladonna Herb (page 42), but the hyoscyne which it contains makes it less likely to give rise to cerebral excitement. Preparations of hyoscyamus are used to counteract the gripping

action of purgatives and to relieve spasm in the urinary tract.

**POISONING.** As for Atropine (page 36).

#### Preparations

HYOSCYAMUS DRY EXTRACT, B.P.C. (page 683)

HYOSCYAMUS LIQUID EXTRACT, B.P.C. (page 683)

GELSEMIUM AND HYOSCYAMUS MIXTURE, COMPOUND, B.P.C. (page 743)

POTASSIUM CITRATE AND HYOSCYAMUS MIXTURE, B.P.C. (page 751)

HYOSCYAMUS TINCTURE, B.P. It contains 0.005 per cent of alkaloids. Dose: 2 to 5 millilitres.

OTHER NAME: Henbane Leaf

## HYPROMELLOSE

SYNONYM: Hydroxypropylmethylcellulose

Hypromellose is a mixed ether of cellulose in which the ether groupings are mainly methoxyl groups with a small proportion of hydroxypropoxyl groups.

Hypromellose may be prepared by reacting alkali cellulose with a mixture of methyl chloride and propylene oxide. The name "hypromellose" is followed by a number indicating the approximate viscosity of a 2.0 per cent solution.

**Solubility.** Soluble in cold water, forming a viscous colloidal solution; insoluble in alcohol, in ether, and in chloroform.

#### Standard

DESCRIPTION; IDENTIFICATION TESTS; ACIDITY OR ALKALINITY; LOSS ON DRYING; SULPHATED ASH. It complies with the tests described under Methylcellulose 20, page 307.

**VISCOSITY.** Determine by the method given for Methylcellulose 20, page 307. The limits for various viscosity grades and the viscometer to be used are indicated in the following table:

Viscosity grade	Viscosity at 20° (centistokes)	Capillary diameter of viscometer (mm)
20	15 to 25	0.84 ± 0.02
50	40 to 60	1.15 ± 0.03
125	110 to 140	1.51 ± 0.03
450	350 to 550	2.06 ± 0.04
1500	1200 to 1800	2.74 ± 0.04
4500	3750 to 5250	3.70 ± 0.04
15,000	12,000 to 18,000	4.97 ± 0.04

**ARSENIC.** It complies with the test given in Appendix 6, page 878 (2 parts per million).

**LEAD.** It complies with the test given in Appendix 7, page 882 (5 parts per million).

**CONTENT OF HYDROXYPROPOXYL.** 4.0 to 7.5 per cent, calculated as  $C_3H_7O_2$ , with reference to the substance dried under the prescribed conditions, determined by the method given in Appendix 22, page 903.

**CONTENT OF METHOXYL.** 27.0 to 30.0 per cent, calculated as  $CH_3O$ , with reference to the substance dried under the prescribed conditions, determined by the method given in Appendix 22, page 903.

**Storage.** It should be stored in airtight containers, in a cool place.

**Uses.** Hypromellose has properties similar to those of methylcellulose, but produces aqueous solutions having higher gel-points and greater clarity; for example, a 2 per cent solution of methylcellulose 4500 gels at about 50° and a 2 per cent solution of hypromellose 4500 gels at about 65°. Because of the greater clarity of aqueous solutions and the lower proportion of undispersed fibres, it is used in preference to methylcellulose to increase the viscosity of ophthalmic solutions; an antimicrobial agent such as benzalkonium chloride should be incorporated.

Hypromellose has also been used in the preparation of anhydrous adhesive ointments for the protection of the skin surrounding ileostomies, fistulas, and exuding ulcers. In the preparation of Plaster of Paris Bandage, hypromellose is used for the same purpose as methylcellulose.

#### Preparation

HYPROMELLOSE EYE-DROPS, B.P.C. (page 692)

## ICHTHAMMOL

SYNONYM: Ammonium Ichthosulphonate

Ichthammol consists mainly of the ammonium salts of the sulphonic acids prepared by sulphonating the oily substances resulting from the destructive distillation of a bituminous schist or shale. It contains, in addition, 5 to 7 per cent of ammonium sulphate.

**Solubility.** Soluble in water; partly soluble in alcohol and in ether; completely soluble in a mixture of equal parts of alcohol and ether.

#### Standard

DESCRIPTION. An almost black, viscid liquid; odour strong and characteristic.



## INDUSTRIAL METHYLATED SPIRIT (ACETONE-FREE)

Industrial Methylated Spirit (Acetone-free) is a mixture, made by a legally authorised methylator, of 19 volumes of alcohol (95 per cent) with 1 volume of approved wood naphtha or other denaturant approved by the Board of Customs and Excise, and is of the quality known as "66 O.P. Industrial Methylated Spirits" but free from acetone.

Other strengths of industrial methylated spirit (acetone-free) are available, such as "Absolute Industrial Methylated Spirits (Acetone-free)", which is 74 O.P., and "64 O.P. Industrial Methylated Spirits (Acetone-free)".

### Standard

**DESCRIPTION.** A colourless, transparent, mobile, volatile liquid; odour of alcohol modified by the odour of the denaturant.

**IDENTIFICATION TEST.** Dilute 0.5 ml to 5 ml with water, add 2 ml of potassium permanganate and phosphoric acid solution, allow to stand for 10 minutes, and add 2 ml of oxalic acid and sulphuric acid solution; to the colourless solution add 5 ml of decolorised magenta solution and allow to stand at 15° to 30° for 30 minutes; a deep violet colour is produced.

**ACIDITY OR ALKALINITY.** 25 ml requires not more than 0.2 ml of 0.1N sodium hydroxide to give a pink colour with phenolphthalein solution, or not more than 1.0 ml of 0.1N hydrochloric acid to give a red colour with methyl red solution.

**SPECIFIC GRAVITY (20°/20°).** Not higher than 0.814.

**ACETONE.** Dilute 5 ml to 10 ml with water, add 1 ml of 2-nitrobenzaldehyde solution followed by 1 ml of a 15 per cent w/v solution of sodium hydroxide in water, and allow to stand for 15 minutes; any colour which develops is not deeper than that produced by 10 ml of a 0.025 per cent v/v solution of acetone in alcohol (50 per cent) when similarly treated (500 parts per million).

**OILY AND RESINOUS SUBSTANCES.** Mix 5 ml with 95 ml of water; the solution remains clear.

**NON-VOLATILE MATTER.** Not more than 0.01 per cent w/v, determined by evaporating to dryness and drying the residue to constant weight at 105°.

**Uses.** Industrial methylated spirit (acetone-free) is used in the preparation of alcoholic solutions of iodine intended for external use.

**UNDESIRABLE EFFECTS; POISONING.** As for Industrial Methylated Spirit (above).

## METHYLCELLULOSE

Methylcellulose is a methyl ether of cellulose. It may be prepared by methylating alkali cellulose with methyl chloride. The name "methylcellulose" is followed by a number indicating the approximate viscosity of a 2.0 per cent solution. The gel-point of a 2 per cent solution in water of Methylcellulose 4500 is about 50°.

**Solubility.** Soluble in cold water, forming a viscous colloidal solution; insoluble in hot water, in alcohol, in ether, and in chloroform.

### Standard

#### METHYLCELLULOSE 20

**DESCRIPTION.** A white or creamy-white powder; odourless.

**IDENTIFICATION TESTS.** 1. Add 1 g to 100 ml of water; the powder swells and disperses, forming a viscous colloidal solution. Boil; a white precipitate is formed which redissolves on cooling.

2. Pour 2 ml of the cold solution prepared in test 1 onto a glass plate and allow the water to evaporate; a thin self-sustaining film is produced.

3. To 10 ml of the cold solution prepared in test 1 add 0.5 ml of a 0.05 per cent w/v solution of brilliant yellow in water, 0.05 ml of 0.1N sodium hydroxide, and 10 ml of a saturated solution of sodium sulphate in water; a voluminous, flocculent, red precipitate is formed. Filter; the filtrate is colourless.

4. Soak in iodine water for a few minutes and remove the excess of reagent; the powder is stained yellow. Add one or two drops of sulphuric acid (86 per cent v/v); it is stained dark brown (distinction from microcrystalline cellulose).

**ACIDITY OR ALKALINITY.** pH of a 1.0 per cent w/v solution in carbon dioxide-free water, 6.0 to 8.0.

**VISCOSITY.** At 20°, 17.0 to 23.0 centistokes, determined by the following method:

Transfer 2.0 g, calculated with reference to the substance dried under the prescribed conditions, to a wide-mouthed bottle, add 100 ml of water previously heated to 85° to 90°, close the bottle with a stopper

fitted with a stirrer, and stir for 10 minutes; place the bottle in an ice-bath, continue stirring until the solution is of uniform consistence, remove the bottle from the ice-bath, and allow the solution to attain room temperature.

Determine the viscosity of this solution by the method of the British Pharmacopoeia, Appendix IVH, for the determination of the viscosity of Methylcellulose, using a suspended-level viscometer with capillary diameter of  $0.84 \pm 0.02$  mm.

**ARSENIC.** It complies with the test given in Appendix 6, page 879 (1 part per million).

**LEAD.** It complies with the test given in Appendix 7, page 883 (5 parts per million).

**LOSS ON DRYING.** Not more than 10.0 per cent, determined by drying to constant weight at 105°.

**SULPHATED ASH.** Not more than 1.0 per cent.

**CONTENT OF METHOXYL.** 27.0 to 29.0 per cent, calculated as  $\text{CH}_3\text{O}$ , with reference to the substance dried under the prescribed conditions, determined by the following method:

Carry out the method of the British Pharmacopoeia, Appendix X(L), for the determination of methoxyl, using about 0.05 g, accurately weighed, and a 25 per cent w/v solution of sodium acetate in the scrubber; each ml of 0.1N sodium thiosulphate is equivalent to 0.0005172 g of  $\text{CH}_3\text{O}$ .

#### METHYLCELLULOSE 450

It complies with the requirements of the British Pharmacopoeia.

It has a viscosity at 20° of 400 to 500 centistokes.



## METHYLCELLULOSE 2500

DESCRIPTION; IDENTIFICATION TESTS; ACIDITY OR ALKALINITY; ARSENIC; LEAD; LOSS ON DRYING; SULPHATED ASH; CONTENT OF METHOXYL. It complies with the tests described under Methylcellulose 20.

VISCOSITY. At 20°, 2200 to 2800 centistokes, determined by the method given above for Methylcellulose 20, a suspended-level viscometer with capillary diameter of  $3.70 \pm 0.04$  mm being used.

## METHYLCELLULOSE 4500

DESCRIPTION; IDENTIFICATION TESTS; ACIDITY OR ALKALINITY; ARSENIC; LEAD; LOSS ON DRYING; SULPHATED ASH; CONTENT OF METHOXYL. It complies with the tests described under Methylcellulose 20.

VISCOSITY. At 20°, 4000 to 5000 centistokes, determined by the method given above for Methylcellulose 20, a suspended-level viscometer with capillary diameter of  $3.70 \pm 0.04$  mm being used.

Storage. Methylcellulose should be stored in airtight containers, in a cool place.

**Actions and uses.** Methylcellulose disperses in cold water to form a viscous colloidal solution. A mucilage may be prepared by adding the methylcellulose to about one-third the required amount of boiling water and, when the powder is thoroughly hydrated, adding the remainder of the water, preferably in the form of ice, and stirring until homogeneous.

Various viscosity grades of methylcellulose are available. High-viscosity grades, such as methylcellulose 2500 and 4500, are used as thickening agents for medicated jellies and

creams, as dispersing agents in suspensions, and as binding and disintegrating agents in tablets. A 0.5 to 1 per cent solution of a high-viscosity grade of methylcellulose is sometimes used to increase the viscosity of ophthalmic solutions, but for this purpose hypromellose (page 232) is usually preferred; an antimicrobial agent such as benzalkonium chloride should be incorporated.

Special grades with a high content of methoxyl, or having hydroxypropyl groups in place of some of the methyl groups (hypromellose, page 232) are used as adhesives in Plaster of Paris Bandage.

A low-viscosity grade, such as methylcellulose 20, is used as an emulsifying agent for liquid paraffin and other mineral oils and also for arachis and olive oils; it is less efficient for emulsifying cod-liver oil. Emulsions are prepared by mixing the oil with a methylcellulose mucilage, preferably using a mechanical stirrer.

Medium- and high-viscosity grades, such as methylcellulose 450, 2500, and 4500, are used as bulk laxatives, usually in the form of granules or tablets.

**Dose.** As a laxative: 1 to 4 grams daily in divided doses.

## Preparation

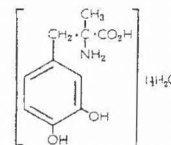
METHYLCELLULOSE GRANULES, B.P.C. (page 703)

OTHER NAMES: *Celacol M*®; *Methocel MC*®

## METHYLDOPA



Methyldopa is the sesquihydrate of (–)-β-(3,4-dihydroxyphenyl)-α-methyl-L-alanine.



**Solubility.** Soluble, at 20°, in 100 parts of water, in 400 parts of alcohol, and in less than 1 part of dilute hydrochloric acid; very slightly soluble in ether.

## Standard

It complies with the requirements of the British Pharmacopoeia.

It is a white to yellowish-white, odourless, fine powder which may contain friable lumps and contains not less than 98.5 and not more than the equivalent of 101.0 per cent of  $\text{C}_{10}\text{H}_{13}\text{NO}_4$ , calculated with reference to the anhydrous substance. It contains 10.0 to 13.0 per cent w/w of water.

**Storage.** It should be stored in airtight containers, protected from light.

**Actions and uses.** Methyldopa inhibits the conversion of dopa to dopamine by competing for the enzyme dopa decarboxylase. In consequence, after the administration of methyldopa there is a reduction in the amount of noradrenaline formed from dopamine, but it has not been proved that this is entirely responsible for its hypotensive effect. Postural hypotension, although it occurs after administration of methyldopa, is never severe,

nor does the blood pressure fall much on exercise.

Methyldopa is used in the treatment of moderate to severe hypertension. A thiazide diuretic may be given concurrently to potentiate the hypotensive effect.

The daily dosage of methyldopa is usually the equivalent of 0.5 to 2 grams of anhydrous methyldopa in divided doses; 1.13 grams of methyldopa is approximately equivalent to 1 gram of anhydrous methyldopa. Occasionally, the daily dosage may be increased to the equivalent of 4 grams.

**UNDESIRABLE EFFECTS.** Tolerance to methyldopa is rarely progressive and can usually be overcome by increasing the dose.

Undesirable effects include drowsiness, depression, dryness of the mouth, diarrhoea, and hyperpyrexia; liver damage, thrombocytopenia, and granulocytopenia have been reported.

Cases of acquired haemolytic anaemia have