HANDBOOK OF PHARMACEUTICAL EXCIPIENTS

THIRD EDITION

EDITED BY

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Hydroxypropyl Methylcellulose

1. Nonproprietary Names

BP: Hypromellose
JP: Hydroxypropylmethylcellulose
PhEur: Methylhydroxypropylcellulosum
USP: Hydroxypropyl methylcellulose

2. Synonyms

Benecel MHPC; Cellulose, hydroxypropyl methyl ether; E464; HPMC; *Methocel*; methylcellulose propylene glycol ether; methyl hydroxypropylcellulose; *Metolose*; *Pharmacoat*.

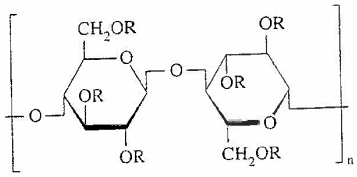
3. Chemical Name and CAS Registry Number

Cellulose, 2-Hydroxypropyl methyl ether [9004-65-3]

4. Empirical Formula Molecular Weight

The PhEur describes hydroxypropyl methylcellulose as a partly *O*-methylated and *O*-(2-hydroxypropylated) cellulose. It is available in several grades which vary in viscosity and extent of substitution. Grades may be distinguished by appending a number indicative of the apparent viscosity, in mPa s, of a 2% w/w aqueous solution at 20°C. Hydroxypropyl methylcellulose defined in the USP specifies the substitution type by appending a four digit number to the nonproprietary name, e.g., hydroxypropyl methylcellulose 1828. The first two digits refer to the approximate percentage content of the methoxy group (OCH_3). The second two digits refer to the approximate percentage content of the hydroxypropoxy group ($OCH_2CHOHCH_3$), calculated on a dried basis. Molecular weight is approximately 10 000-1 500 000.

5. Structural Formula



Where R is H, CH_3, or $[CH_3CH(OH)CH_2]$.

6. Functional Category

Coating agent; film-former; rate-controlling polymer for sustained release; stabilizing agent; suspending agent; tablet binder; viscosity-increasing agent.

7. Applications in Pharmaceutical Formulation or Technology

Hydroxypropyl methylcellulose is widely used in oral and topical pharmaceutical formulations.

In oral products, hydroxypropyl methylcellulose is primarily used as a tablet binder,[1] in film-coating,[2-7] and as an extended-release tablet matrix.[8-12] Concentrations of between 2-5% w/w may be used as a binder in either wet- or dry-granulation processes. High viscosity grades may be used to retard the release of drugs from a matrix at levels 10-80% w/w in tablets and capsules.

Depending upon the viscosity grade, concentrations between 2-20% w/w are used as film-forming solutions to film-coat tablets. Lower viscosity grades are used in aqueous film-coating solutions while higher viscosity grades are used with organic solvents.

Hydroxypropyl methylcellulose is also used as a suspending and thickening agent in topical formulations, particularly ophthalmic preparations. Compared with methylcellulose, hydroxypropyl methylcellulose produces solutions of greater clarity, with fewer undispersed fibers present, and is therefore preferred in formulations for ophthalmic use. Concentrations of between 0.45-1.0% w/w may be added as a thickening agent to vehicles for eye drops and artificial tear solutions.

Hydroxypropyl methylcellulose is also used as an emulsifier, suspending agent, and stabilizing agent in topical gels and ointments. As a protective colloid, it can prevent droplets and particles from coalescing or agglomerating, thus inhibiting the formation of sediments.

In addition, hydroxypropyl methylcellulose is used in the manufacture of capsules, as an adhesive in plastic bandages and as a wetting agent for hard contact lenses. It is also widely used in cosmetics and food products.

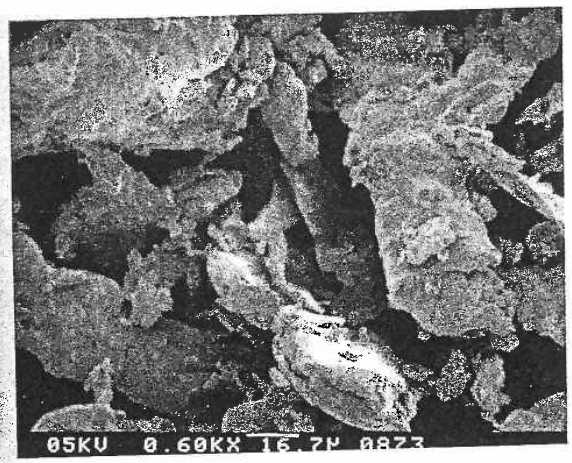
8. Description

Hydroxypropyl methylcellulose is an odorless and tasteless, white or creamy-white colored fibrous or granular powder.

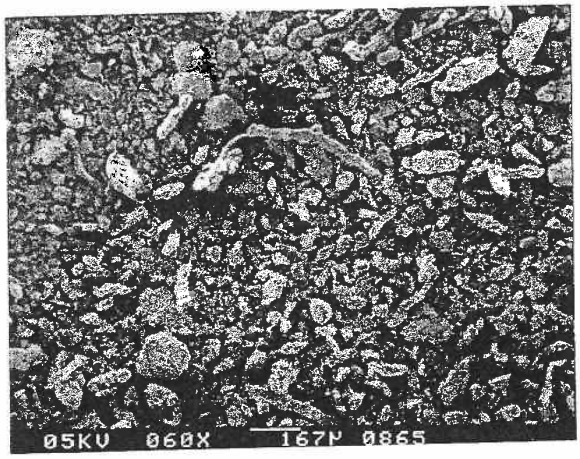
9. Pharmacopeial Specifications

Test	JP	PhEur	USP
Identification	+	+	+
Appearance of solution	+	+	—
pH (1% w/w solution)	5.0-8.0	5.5-8.0	—
Apparent viscosity	+	+	+
Loss on drying	≤ 5.0%	≤ 10.0%	≤ 5.0%
Residue on ignition			
For viscosity grade > 50 mPa s	≤ 1.5%	—	≤ 1.5%
For viscosity grade ≤ 50 mPa s	≤ 1.5%	—	≤ 3.0%
For type 1828 of all viscosities	≤ 1.5%	—	≤ 5.0%
Sulfated ash	—	≤ 1.0%	—
Chlorides	—	≤ 0.5%	—
Heavy metals	—	≤ 20 ppm	≤ 0.001%
Methoxy content			
Type 1828	—	—	16.5-20.0%
Type 2208	19.0-24.0%	—	19.0-24.0%
Type 2906	27.0-30.0%	—	27.0-30.0%
Type 2910	28.0-30.0%	—	28.0-30.0%
Hydroxypropoxy content			
Type 1828	—	—	23.0-32.0%
Type 2208	4.0-12.0%	—	4.0-12.0%
Type 2906	4.0-7.5%	—	4.0-7.5%
Type 2910	7.0-12.0%	—	7.0-12.0%

SEM: 1
Excipient: Hydroxypropyl methylcellulose
Manufacturer: Dow Chemical Co
Lot No.: ME20012N11
Magnification: 600×
Voltage: 5kV



SEM: 2
Excipient: Hydroxypropyl methylcellulose
Manufacturer: Dow Chemical Co
Lot No.: ME20012N11
Magnification: 60×
Voltage: 5kV



10. Typical Properties

Acidity/alkalinity:
pH = 5.5-8.0 for a 1% w/w aqueous solution.
Ash: 1.5-3.0%, depending upon the grade.
Autoignition temperature: 360°C
Density (bulk): 0.341 g/cm^3
Density (tapped): 0.557 g/cm^3
Density (true): 1.326 g/cm^3
Melting point: browns at 190-200°C; chars at 225-230°C. Glass transition temperature is 170-180°C.
Moisture content: hydroxypropyl methylcellulose absorbs moisture from the atmosphere, the amount of water absorbed depending upon the initial moisture content and the temperature and relative humidity of the surrounding air. *See* Fig. 1.
Particle size distribution: *See* Table I.
Solubility: soluble in cold water, forming a viscous colloidal solution; practically insoluble in chloroform, ethanol (95%), and ether, but soluble in mixtures of ethanol and dichloromethane, mixtures of methanol and dichloromethane, and mixtures of water and alcohol. Certain grades of hydroxypropyl methylcellulose are soluble in aqueous acetone solutions, mixtures of dichloromethane and propan-2-ol, and other organic solvents. *See also* Section 11.
Specific gravity: 1.26
Viscosity (dynamic): a wide range of viscosity types are commercially available. Aqueous solutions are most commonly prepared although hydroxypropyl methylcellulose may also be dissolved in aqueous alcohols such as ethanol and propan-2-ol provided the alcohol content is less than 50% w/w. Dichloromethane and ethanol mixtures may also be used to prepare viscous hydroxypropyl methylcellulose solutions. Solutions prepared using organic solvents tend to be more viscous; increasing concentration also produces more viscous solutions, *see* Table II.

To prepare an aqueous solution, it is recommended that hydroxypropyl methylcellulose is dispersed and thoroughly hydrated in about 20-30% of the required amount of water. The water should be vigorously stirred and heated to 80-90°C then the remaining hydroxypropyl methylcellulose added. Cold water should then be added to produce the required volume.

When a water-miscible organic solvent such as ethanol, glycol, or mixtures of ethanol and dichloromethane is used, the hydroxypropyl methylcellulose should first be dispersed into the organic solvent, at a ratio of 5-8 parts of solvent to 1 part of hydroxypropyl methylcellulose. Cold water is then added to produce the required volume.

Table I: Typical particle size distribution for hydroxypropyl methylcellulose.

	Average particle size (μm)	Cumulative frequency oversize (%)	Weight retained (%)
Lot LC15012N11	250	5.6	5.60
	200	18.8	13.20
	137	26.6	7.8
	115	35.4	8.8
	90	54.4	19.0
	64	85.8	31.4
	pan	100	14.0
Lot LA29012N02	250	2.8	2.8
	200	15.6	12.8
	137	20.6	5.0
	115	26.4	5.8
	90	42.8	16.4
	64	68	25.2
	pan	100	33

Note: Using an ATM Sonic Softener.

11. Stability and Storage Conditions

Hydroxypropyl methylcellulose powder is a stable material although it is hygroscopic after drying.

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