# Microcrystalline Cellulose

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This draft proposal contains monograph text for inclusion in the Indian Pharmacopoeia (IP). The content of this draft document is not final, and the text may be subject to revisions before publication in the IP. This draft does not necessarily represent the decisions or the stated policy of the IP or Indian Pharmacopoeia Commission (IPC).

Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

**Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.**

## Document History and Schedule for the Adoption Process

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| Further follow-up action as required. | |

# **Microcrystalline Cellulose**. Page 2937

Change **to:** **Microcrystalline Cellulose**

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*This monograph has been harmonized with corresponding texts of the European Pharmacopoeia, the Japanese Pharmacopoeia and the United States Pharmacopeia. Portions of the IP text that and are not part of the PDG harmonized text, are marked with symbols* (♦ ♦).

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Microcrystalline Cellulose is purified, partially depolymerized cellulose prepared by treating alpha cellulose, obtained as a pulp from fibrous plant material, with mineral acids.

♦Microcrystalline Cellulose contains not less than 97.0 per cent and not more than 102.0 per cent of cellulose, calculated on the dried basis.♦

♦**Category**. Pharmaceutical aid.♦

♦**Description**. A fine or granular, white or almost white powder.♦

## Identification

A. Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *microcrystalline cellulose IPRS* or with the reference spectrum of microcrystalline cellulose.

*NOTE – Disregard any peak obtained between 800 $cm^{-1}$ to 825 $cm^{-1}$ and between 950 $cm^{-1}$ to 1000 $cm^{-1}$.*

B. Place 10 mg of the substance under examination on a watch-glass and dissolve in 2 ml of *iodinated zinc chloride solution*; a blue-violet colour is produced.

C. Transfer 1.3 g to a 125-ml conical flask, add 25 ml of *water* and 25 ml of 1 M cupriethylenediamine hydroxide solution. Immediately purge the solution with nitrogen, stopper the flask, and shake until completely dissolved. Transfer an appropriate volume of the solution to a suitable capillary viscometer (2.4.28). Allow to solution to equilibrate at 25 ± 0.1° for 5 minutes. Record the flow time in seconds ($t_1$) between the 2 marks on the viscometer.

Determine the kinematic viscosity ($v_1$) of the solution using following expression:

$$\text{Result} = t_1 \times k_1$$

where, $k_1$ = viscometer constant,
$t_1$ = flow time (in seconds).

Mix an equal volume of *water* and 1 M cupriethylenediamine hydroxide solution, and determine the flow time in seconds ($t_2$).

Determine the kinematic viscosity ($v_2$) of the solvent using following expression:

$$\text{Result} = t_2 \times k_2$$

where, $k_2$ = viscometer constant,
t2 = flow time for 0.5 M cupriethylenediamine hydroxide solution (in seconds).

Determine the relative velocity ($\eta_{rel}$) of the substance under examination using the following expression:

$$\text{Relative velocity } (\eta_{rel}) = \frac{v_1}{v_2}$$

where, v1 = kinetic velocity of microcrystalline cellulose taken,
v2 = kinetic velocity of solvent.

Determine the intrinsic viscosity $[\eta]_c$ by interpolation using the intrinsic viscosity table.

Calculate the degree of polymerization (P) using the following expression:

$$P = \frac{95 \times [\eta]_c}{W \times [(100 - LOD) / 100]}$$

where, W = weight of the substance under examination (in g),
LOD = loss on drying in per cent.

The degree of polymerization is not more than 350.

## Tests

**pH** (2.4.24). 5.0 to 7.5 determined in the supernatant obtained by shaking 5.0 g with 40 ml of *water* for 20 minutes and centrifuging.

**Bulk density** (2.4.35). Not more than the stated labelled value determined using *Method II*.

**Conductivity** (2.4.9). Determine the conductivity of the supernatant obtained in the pH test, using an appropriate conductivity meter that has been standardized with a potassium chloride conductivity calibration standard having a conductivity of 100 µS per cm. Measure the conductivity of the supernatant after a stable reading is obtained and measure the conductivity of the water used to prepare the test specimen. The conductivity of the supernatant does not exceed the conductivity of the *water* by more than 75 µS per cm.

**Ether-soluble substances**. Place 10.0 g in a chromatographic column of 20 mm internal diameter and pass 50 ml of *peroxide-free ether* through the column. Evaporate the eluate to dryness into a tared beaker with the aid of a current of air in a fume hood. After all the ether has evaporated, dry the residue at 105° for 30 minutes. The difference between the weight of the residue and the weight obtained from a blank determination does not exceed 5.0 mg (0.05 per cent).

**Water-soluble substances**. Shake 5.0 g with about 80 ml of *water* for 10 minutes, filter through a filter paper (Whatman No 42 or equivalent) into a tared beaker and evaporate the filtrate to dryness without charring and dry the residue at 105° for 1 hour. The residue weighs not more than 12.5 mg (0.25 per cent).

♦**Arsenic** (2.3.10). Mix 5.0 g with 3 g of *anhydrous sodium carbonate*, add 10 ml of *bromine solution* and mix thoroughly. Evaporate to dryness on a water-bath, gently ignite and dissolve the cooled residue in a mixture of 15 ml of *hydrochloric acid* containing 0.15 ml of *bromine solution* and 45 ml of *water*. Add 2 ml of *stannous chloride solution AsT*. The resulting solution complies with the limit test for arsenic (2 ppm).♦

**Sulphated ash** (2.3.18). Not more than 0.1 per cent, determined on 1.0 g.

**Loss on drying** (2.4.19). Not more than 7.0 per cent, or some other lower percentage, or is within a percentage range as specified in the labelling.

**Microbial contamination** (2.2.9). Total aerobic viable count is not more than $10^3$ CFU per g and total fungal count is not more than$10^2$ CFU per g determined by plate count. 1 g is free from *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Salmonella*.

♦**Assay**. Weigh 0.125 g and transfer to a 300-ml conical flask with the aid of about 25 ml of *water*. Add 50.0 ml of *0.083 M potassium dichromate*, mix, carefully add 100 ml of *sulphuric acid* and heat to boiling. Remove from heat, allow to stand at room temperature for 15 minutes, cool and transfer to a 250-ml volumetric flask. Dilute with *water* almost to volume, cool to 25°, dilute with *water* to volume and mix. Titrate 50.0 ml of the resulting solution with *0.1 M ferrous ammonium sulphate* using 2 to 3 drops of *ferroin sulphate solution* as indicator. Repeat the procedure without the substance under examination. The difference between the titrations represents the amount of ferrous ammonium sulphate required.

1 ml of *0.1 M ferrous ammonium sulphate* is equivalent to 0.000675 g of cellulose.♦

♦**Storage**. Store protected from moisture.♦

**Labelling**. The label states nominal loss on drying, bulk density and degree of polymerization values. Degree of polymerization compliance is determined using Identification C. Where the particle size distribution is stated in the labeling, proceed as directed in the test for Particle Size Distribution. The labeling indicates with which technique the particle size distribution was determined if a technique other than analytical sieving was used; and the labeling indicates the $d_{10}$, $d_{50}$ and $d_{90}$ values and the range for each.