

Draft Proposal for Comments and Inclusion in The Indian Pharmacopoeia

Melatonin

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This draft proposal contains general chapter 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).

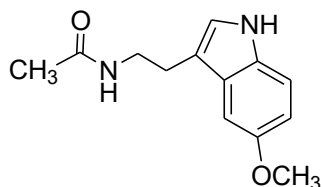
Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to arnd-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

Description	Details
Document version	1.0
Monograph proposed for inclusion	Addendum to IP 2026
Tentative effective date of monograph	April, 2028
First draft published on IPC website for public comments	
Draft revision published on IPC website for public comments	
Further follow-up action as required.	

Melatonin



$C_{13}H_{16}N_2O_2$

Mol. Wt. 232.3

Melatonin is *N*-(2-(5-methoxy-1*H*-indol-ethyl) acetamide).

Melatonin contains not less than 98.5 per cent and 101.5 per cent of $C_{13}H_{16}N_2O_2$, calculated on dried basis.

Category. Melatonin receptor agonist.

Description. A white to slightly yellowish powder.

Identification

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

B. In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with reference solution (a).

Tests

Related Substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 25 volumes of mobile phase A and 75 volumes of mobile phase B.

Test Solution. Dissolve 25.0 mg of the substance under examination in the solvent mixture and dilute to 25.0 ml with the solvent mixture.

Reference solution (a). A 0.0005 per cent w/v solution of *melatonin IPRS* in the solvent mixture.

Reference solution (b). A solution containing 0.01 per cent w/v of *melatonin IPRS* and 0.002 per cent w/v of *melatonin related compound A IPRS* (2-(5-methoxy-1*H*-indol-3-yl)ethanamine) in the solvent mixture.

Chromatographic system

– a stainless steel column 15 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 μ m) (such as Kromasil ODS),

– mobile phase: A. *acetonitrile*,

B. a buffer solution prepared by dissolving 0.5 g of *potassium dihydrogen orthophosphate* in 1000 ml of *water*, adjusted to pH 3.5 with *orthophosphoric acid*,

– a gradient programme using the conditions given below,

– flow rate: 1 ml per minute,

– spectrophotometer set at 222 nm,

– injection volume: 10 μ l.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile Phase B (per cent v/v)
0	25	75
7	25	75
15	80	20
18	25	75
25	25	75

The relative retention time with reference to melatonin for melatonin related compound A is about 0.4.

Inject reference solution (b). The test is not valid unless the resolution between the peaks due to melatonin related compound A and melatonin is not less than 4.0 and the relative standard deviation of replicate injections is not more than 2.0 per cent for the melatonin peak.

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any secondary peak is not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent) and the sum of the areas of all the secondary peaks is not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (1.0 per cent).

Chlorides (2.3.12). 1.25 g complies with the limit test for chlorides (200 ppm).

Sulphated ash (2.3.18). Not more than 0.1 per cent.

Loss on drying (2.4.19). Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 80° for 3 hours.

Assay. Determine by liquid chromatography (2.4.14).

Test Solution. Dissolve 25.0 mg of the substance under examination in the mobile phase and dilute to 250.0 ml with the mobile phase.

Reference solution (a). A 0.01 per cent w/v solution of *melatonin IPRS* in the mobile phase.

Reference solution (b). A solution containing 0.01 per cent w/v of *melatonin IPRS* and 0.002 per cent w/v of *melatonin related compound A IPRS* (2-(5-methoxy-1H-indol-3-yl)ethanamine) in the mobile phase.

Chromatographic system

- a stainless steel column 15 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (such as Kromasil ODS),
- mobile phase: a mixture of 25 volumes of *acetonitrile* and 75 volumes of a buffer prepared by dissolving 0.5 g of *potassium dihydrogen orthophosphate* in 1000 ml of *water*, adjusted to pH 3.5 with *orthophosphoric acid*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 222 nm,
- injection volume: 10 µl.

The relative retention time with reference to melatonin for melatonin related compound A is about 0.4.

Inject reference solution (a) and (b). The test is not valid unless the resolution between the peaks due to melatonin and melatonin related compound A is not less than 4.0 in the chromatogram obtained with reference solution (b) and the relative standard deviation for replicate injections is not more than 2.0 per cent in the chromatogram obtained with reference solution (a).

Inject reference solution (a) and the test solution.

Calculate the content of C₁₃H₁₆N₂O₂.

Storage. Store protected from light and moisture at a temperature not exceeding 30°.

Solubility. Slightly soluble in *water*, soluble in *ethanol* (95 per cent), sparingly soluble in *ethyl acetate* and practically insoluble in *heptane*.