

Draft Proposal for Comments and Inclusion in The Indian Pharmacopoeia

Croscarmellose Sodium

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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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Draft revision published on IPC website for public comments	--
Further follow-up action as required.	

Croscarmellose Sodium. Page 1965Change to: **Croscarmellose Sodium**

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 are not part of the PDG harmonized text, are marked with symbols (◆◆).

Croscarmellose sodium (cross-linked sodium carboxymethyl cellulose) is the sodium salt of a cross-linked, partly *O*-carboxymethylated cellulose.

◆**Category.** Pharmaceutical aid.

Description. A white or grayish-white powder.◆

Identification

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

NOTE – Depending on the degree of substitution, the intensity of the absorption band at about 1750 cm⁻¹ may vary.

B. Mix 1 g with 100 ml of 0.0004 per cent w/v solution of *methylene blue*, stir the mixture and allow to settle. The substance under examination absorbs the methylene blue and settles as a blue fibrous mass.

C. The solution prepared by dissolving a portion of residue from the sulphated ash in 2 ml of *water* gives reaction (A) of sodium salts (2.3.1).

Tests

pH (2.4.24). 5.0 to 7.0, determined on 1.0 per cent w/v solution in *water*, after shaking for 5 minutes.

Degree of substitution. Take 1.0 g in 500 ml conical flask, add 300 ml of a 10 per cent w/v solution of *sodium chloride*, 25.0 ml of 0.1 *M sodium hydroxide*, stopper the flask and allow to stand for 5 minutes, shaking occasionally. Add 0.05 ml of *m-cresol purple solution* and about 15 ml of 0.1 *M hydrochloric acid* from a burette. Insert the stopper and shake. If the solution is violet, add 0.1 *M hydrochloric acid* in 1 ml portions until the solution becomes yellow, shaking after each addition. Titrate with 0.1 *M sodium hydroxide* until the colour turns to violet.

Calculate the number of milliequivalents (*M*) of base required for the neutralisation equivalent to 1 g of dried substance.

Calculate the degree of acid carboxymethyl substitution (*A*) using the following expression:

$$\frac{1150 \times M}{[7102 - (412 \times M) - (80 \times C)]}$$

where, *M* = milliequivalent of base,

C = percentage of sulphated ash.

Calculate the degree of sodium carboxymethyl substitution (*S*) using the following expression:

$$\frac{[162 + (58 \times A)] \times C}{[7102 - (80 \times C)]}$$

where, *A* = degree of acid carboxymethyl substitution,

C = percentage of sulphated ash.

The degree of substitution is the sum of *A* + *S* and it is 0.60 to 0.85, calculated on the dried basis.

◆**Sodium chloride and sodium glycollate.** The sum of the percentage contents of sodium chloride and sodium glycollate is not more than 0.5 per cent, calculated on the dried basis.

Sodium chloride. Transfer 5.0 g of the substance under examination to a 250- ml conical flask, add 50 ml of *water* and 5 ml of *strong hydrogen peroxide solution* and heat on a water-bath for 20 minutes stirring occasionally to ensure total hydration. Cool, add 100 ml of *water* and 10 ml of *nitric acid*. Titrate with 0.05 *M silver nitrate* determining the end-point

potentiometrically (2.4.25) using a silver indicator electrode and a double-junction reference electrode containing 10 per cent w/v solution of *potassium nitrate* in the outer jacket and a standard filling solution in the inner jacket, and stirring constantly.

1 ml of 0.05 M *silver nitrate* is equivalent to 0.002922 g of NaCl.

Sodium glycollate.

Test Solution. Transfer 0.5 g of the substance under examination to a 100- ml beaker, add 5 ml of *glacial acetic acid* and 5 ml of *water* and stir to ensure total hydration (about 15 minutes). add 50 ml of *acetone* and 1 g of *sodium chloride*. stir for several minutes to ensure complete precipitation of the carboxymethyl cellulose. Filter through a soft opened textured paper filter paper previously wetted with small amount of *acetone* and collect the filtrate in a 100- ml volumetric flask. Use an additional 30 ml of *acetone* to facilitate the transfer of the solids and to wash the filter cake then dilute to volume with *acetone* and mix.

Reference solution. Dissolve 0.1 g of *glycollic acid* in 100 ml of *water*. Use the solution within 30 days. Transfer 1.0 ml, 2.0 ml, 3.0 ml and 4.0 ml of the solution to separate volumetric flasks; dilute the contents of each flask to 5.0 ml with *water*, add 5 ml of *glacial acetic acid*, dilute to 100.0 ml with *acetone* and mix.

Transfer 2.0 ml of the test solution and 2.0 ml of each of the reference solutions to separate 25 ml volumetric flasks. Heat the uncovered flasks for 20 minutes on a water-bath to eliminate *acetone*. Allow to cool and add 5.0 ml of 2,7-*dihydroxynaphthalene solution* to each flask. Mix, add a further 15.0 ml of 2,7-*dihydroxynaphthalene solution* and mix again. Close the flasks with aluminium foil and heat on a water-bath for 20 minutes. Cool and dilute to 25.0 ml with *sulphuric acid*.

Measure the absorbance (2.4.7) of each solution at 540 nm. Prepare a blank using 2.0 ml of a solution containing 5 per cent v/v each of *glacial acetic acid* and *water* in *acetone*. Prepare a standard curve using the absorbances obtained with the reference solutions. From the standard curve and the absorbance of the test solution, determine the mass, in milligrams, of glycollic acid in the substance under examination and calculate the content of sodium glycollate from the expression:

$$\frac{10 \times 1.29 \times a}{(100 - b) w}$$

where, 1.29 = the factor converting glycollic acid to sodium glycollate,

a = mass of the *glycollic acid* in the specimen determined from the standard curve and the absorbance of the test solution, in grams,

b = loss on drying as a percentage,

w = mass of the substance under examination, in grams ♦

Water-soluble substances. Not more than 10.0 per cent.

Disperse 10.0 g in 800.0 ml of *water* and stir for 1 minute every 10 minutes during the first 30 minutes. Allow to stand for 1 hour and centrifuge, if necessary. Decant 200.0 ml of the aqueous slurry on to a fast filter paper in a vacuum filtration funnel, apply vacuum and collect 150.0 ml of the filtrate. Pour the filtrate into a tarred 250-ml beaker, weigh and calculate the weight, in g, of the filtrate (w_3), by difference. Concentrate on a hot plate to a small volume but not to dryness, dry at 105° for 4 hours and again weigh. Calculate the weight of the residue by difference (w_1).

Calculate the percentage of water soluble material, on the dried basis.

$$\text{Water soluble material} = \frac{[100 \times w_1 \times (800 + w_2)]}{\{w_2 \times w_3 \times [1 - (0.01 \times b)]\}}$$

where, w_1 = weight of the residue by difference, in grams,

w_2 = weight of substance under examination, in grams,

w_3 = weight of the filtrate by difference, in grams,

b = loss on drying as percentage.

Settling volume. 10.0 to 30.0 ml. Place 75 ml of *water* in a 100 ml graduated cylinder and add 1.5 g of the substance under examination in 0.5 g portions, shaking vigorously after each addition, dilute to 100.0 ml with *water* and shake again until the substance is homogeneously distributed. Allow to stand for 4 hours. Note the volume of the settled mass.

♦**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*. ♦

Sulphated ash (2.3.18). 14.0 to 28.0 per cent, calculated on the dried basis.

Loss on drying (2.4.19). Not more than 10.0 per cent, determined on 1.0 g by drying in an oven at 105° for 6 hours.

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

Solubility. Practically insoluble in *ethanol*, in *acetone* and in *toluene*.

Draft for Comments