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# CHLORINE DETERMINATION IN MODIFIED CELLULOSE PHARMACEUTICAL EXCIPIENTS BY ICP-OES AFTER PYROYDROLYSIS SAMPLE PREPARATION

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Modified cellulose, as hydroxypropyl methylcellulose (HPMC) and carboxy methylcellulose (CMC) has been used as excipients in pharmaceutical formulations.[1] Despite of the extensive use of these compounds, excipients are not completely free of impurities and the quality control is mandatory. In modified cellulose, chlorine (a byproduct during chemical modification) determination is required as a limit test. According to the European Pharmacopeia (EP), chlorine concentration in HPMC must be lower than 0.5%. In EP, chlorine is qualitatively detected in a limit test that consists of a reaction of chlorine with $AgNO_3$ after previous sample solubilization in diluted $HNO_3$. The turbidity is visually compared with a chlorine standard.[1] The main disadvantages of this method are the difficult of all chlorine species react during the limit test and the possibility of occurrence of erroneous results due to the analyst subjective ability for comparison of the solutions, especially at low concentrations. In order to solve this problem, a homemade pyrohydrolysis system was developed as sample preparation system for further chorine determination in modified cellulose. Pyrohydrolysis consists in the pyrolysis of samples in the presence of water vapor, followed by hydrolysis of chlorine as well as other halogens in its respective volatile acid. These volatile species can be condensed and collected in water or alkaline solutions. In the present work, the determination of chlorine was performed by inductively coupled plasma optical emission spectrometry (ICP-OES) using axial view (Ciros CCD, Spectro Analytical Instruments, Germany) at 134.724 nm. The pyrohydrolysis conditions were optimized using a HPMC sample, evaluating the sample mass (100 to 500 mg), oxygen flow rate (0.1 to 0.4 L $min^{-1}$), absorbing solution (water or 10 to 100 mmol $L^{-1}$ $NH_4OH$), volume of absorbing solution (6 and 10 mL) and reaction time (1 to 15 min). Using the pyrohydrolysis system it was possible to digest up to 500 mg of sample. The best conditions were 6 mL of 25 mmol $L^{-1}$ $NH_4OH$ as absorbing solution and oxygen flow rate of 0.4 L $min^{-1}$, during 5 min. The limit of detection was 15 μg $g^{-1}$. Accuracy was evaluated by comparison of the results with those obtained after microwave-induced combustion (MIC) and determination by ICP-OES, and no statistical difference was observed. Chlorine was determined in HPMC (3 samples) and CMC (1 sample) and concentrations ranged from 285 to 272 μg $g^{-1}$. These results showed the suitability of pyrohydrolysis as sample preparation method for chlorine determination in modified cellulose pharmaceutical excipients.

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**References:**

1 European Pharmacopeia, 5ª edition, Volume 1, 2005.