Alternative method for chloride and sulphate determination in inorganic drugs by IC after volatilization by MIC

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Abstract

Chloride and sulphate determination from inorganic drugs was proposed by IC, after volatilization by MIC.

Introduction

The presence of inorganic impurities in inorganic drugs, even in low concentrations, promoting great risk to users. In view of this, the quality of drugs and active pharmaceutical ingredient (API) was ensured by tests described in Pharmacopoeias.[1] The calcium carbonate is an example of API used in inorganic drugs applied to relief of gastric hyperacidity or for calcium supplementation in the human organism.[1] In these drugs quantification of Cl^- and SO_4^{2-} are based on a visual comparison.[1,2] Despite its relative simplicity and low cost, these tests are semi-quantitative.[1] However, sample preparation methods for inorganic matrices is a challenge. Thus, this study aims to propose method for Cl^- and SO_4^{2-} from $CaCO_3$ drugs using volatilization by microwave-induced combustion (MIC), after determination by ion chromatography (IC).

Results and Discussion

The pharmaceutical products constituted of $CaCO_3$ (API and excipient) were obtained from industries at Brazil. After grinding, the samples were dried in an oven at 60 ºC for 4 h. In the volatilization method, conduced in a microwave oven (Multiwave 3000™, Anton Paar), the sample (400 to 1200 mg), wrapped in polyethylene film, was combusted in closed quartz vessels pressurized with oxygen (20 bar). Microcrystalline cellulose (100 to 200 mg) was evaluated as an aid of volatilization, being mixed with the sample. Ultrapure water, the eluent used in IC analysis (3.2 Na_2CO_3/1.0 $NaHCO_3$), $(NH_4)_2CO_3$ (50 mmol l^{-1}) or NH_4OH (50 mmol l^{-1}) were evaluated as absorbing solution. The irradiation program used was: 1400 W for 50 s, 0 W for 2 min, 1400 W for 5 min and 0 W for 20 min (cooling). After the combustion, the resultant solutions were diluted with ultrapure water to 25 ml for further determination of Cl^- and SO_4^{2-} by IC (861 advanced compact IC, Metrohm). The accuracy of the method was performed by spike recovery using standard reference materials (SRM) NIST 1547 (Peach leaves) and NIST 8433 (Corn Bran), which were mixed to the samples, before to decomposition procedure. The API and the drug analysed present the ash content of around 60 and 25% respectively. Whereas that ash content was possible to estimate to $CaCO_3$ (100 and 45% respectively). Thus, the better condition for analytes volatilization was achieved by using 600 mg of the drug, without aid volatilization. However, for decomposition of API, was selected as better condition the mixture of 300 mg of sample with 300 mg of cellulose. Ultrapure water was selected for analytes absorption after volatilization, considering the absence of interferences, lower relative standard deviations (RSDs), reduced cost of analysis and lower waste generation. The limits of detection (LODs) for Cl^- and SO_4^{2-} using the proposed method were 7.5 and 13.7 mg kg^{-1}, respectively. Five drugs containing $CaCO_3$ were analyzed by the proposed method, and obtained concentrations for Cl^- and SO_4^{2-} ranged from 55 to 71 mg kg^{-1}, and from 62 to 117 mg kg^{-1}, respectively. However, when the API was analyzed, the concentrations for both analytes were lower than LOD, which allow to relate Cl^- and SO_4^{2-} content with presence of the excipients. These values were in agreement with Brazilian Pharmacopoeia recommendations.[1] The analysis of SRMs as a spike recovery confirmed the good accuracy for Cl^- and SO_4^{2-}, with analytes recoveries between 95 and 101%. Additionally, RSDs for both analytes were always lower than 6%.

Conclusion

The proposed method using volatilization by MIC before IC determination was appropriate for Cl^- and SO_4^{2-} determination in pharmaceutical products constituted of $CaCO_3$. The obtained analyte concentrations in drugs were in agreement with Pharmacopoeia recommendations.[1] Therefore, the proposed method can be one alternative when compared to Pharmacopoeia methods.

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[1]BRASIL, Farmacopeia Brasileira, 5ª Ed, volume 1 e 2, Agência Nacional de Vigilância Sanitária, 2010.

[2]ICH: International Conferences on Harmonization, Draft Revised Guidance on Impurities in New Drug Substances. Q3A(R). Federal Register; 65(140):45085-45090, 2000.