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Short communication

Potentiometric determination of calcium content with combined Cu ISE and reference Ag/AgCl electrode in API

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Introduction

There are numerous methods for determination of metal ions and other inorganic species in API. In the last years, there have been cases of hypercalcemia as conditions from a long-term medical therapy. From here goes the interest for better controlling of their intake with API that contain the metal ions in their composition. Because of its importance and uses in all areas of a human body (nervous system, muscles, heart and bone), a complexometric potentiometric method is suggested and tested for determination of Ca ions.

Calcium content in analyzed in Atorvastatin Calcium x $3H_2O$, an API. Atorvastatin Ca x $3H_2O$ is the calcium salt of atorvastatin, used as a synthetic lipid-lowering agent. The calcium content of the active component has limits from 3.2% to 3.8% (on anhydrous and solvent free basis).

The titration proposed for this determination is performed using combined Cu ISE and reference Ag/AgCl electrode. The method is based, on a complexometric titration with 0.1M EDTA as a volumetric solution, which forms a complex with calcium ions.

The purpose of this determination was implementing potentiometric method in our laboratories.

Materials and methods

Reagents

-1N Hydrochloric acid
-Methanol (Merck)
-Volumetric solution: EDTA-ethylenediaminetetraacetic acid solution 0.1M - Titriplex (Merck)
-$CaCO_3$: Chelometric standard dried at 110°C using laboratory oven for 2 hours
-Cu-Complex: 0.05M CuEDTA prepared accurate: 1:1 mixture of 0.1M CuSO4 and 0.1M EDTA volumetric solutions
-Ammonia Buffer: mix (pH about 10): 54g NH_4Cl and 350mL NH_4OH 25% in 1000mL

Potentiometer Metrohm 888 Titrando instrument with Tiamo software and 0.1M EDTA burette was used for the potentiometric titration and analytical balance Mettler Tolledo was used for weighting the samples. The samples were dried in laboratory Oven Binder. The titration was performed using Metrohm 6.0502.140 Cu ISE with 6.0733.100 reference electrode (Ag/AgCl).

Procedures for Ca determination

Factorization of 0.1M solution EDTA

From the chelometric-dried standard, three samples (around 100mg) were prepared in 100 mL glass beaker. Magnetic stirrers were used for dissolving the standard with 10 mL distilled water and 3 mL 1N HCl. After that, 40 mL water was added and mixed well. Then, 5 mL of the prepared Buffer and 1 mL of CuEDTA complex were added.
This formula was used for calculations:

$$Factor = \frac{weight\ Calcium\ carborante\ (mg)}{(V_{titrant} - V_{blank})\ x\ 0.1\ x\ 100.09}$$

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$V_{titrant}$ – Volume consumed for End Point (EP) criteria in sample
V_{blank} – Volume consumed for blank determination
100.09 – molar mass of $CaCO_3$
0.1 – normality of volumetric solution
weight of $CaCO_3$ – exact weight in mg

Blank titration was performed.

Calcium determination in API

Two samples and a blank determination are prepared. Samples weight is approximately 500 mg of Atorvastatin Ca x $3H_2O$ in 100 mL glass baker. The samples were dissolved with magnetic stirrer and 50 mL of Methanol. After that, 10 mL Ammonia buffer and 2 mL CuEDTA complex were added.
The following formula was used for calculations:

$$\%\ Calcium = \frac{(V_{titrant} - V_{blank})\ \text{x}\ 0.1\ \text{x}\ F_{titrant}\ \text{x}\ 40.078}{\text{weight sample (mg)}}\ x\ 100$$

$V_{titrant}$ – Volume consumed for EP criteria in sample
V_{blank} – Volume consumed for blank determination
40.078 – Ca molar mass
0.1 – normality of volumetric solution
Weight sample – exact weight in mg

The parameters of the method were as follows:
-Mode – MET U;
-EP Criterion – 20mV (for titer and for sample), for blank titer 10mV ;
-EP recognition – Greatest;
-Stirring rate – 4;
-Volume increment for sample and for the blank - 0.1mL sample and 0.002mL, respectively;
-minimum waiting time – 10 s;
-maximum waiting time – 20 s;
-signal drift – 20 mV (for sample and for blank), 40mV (titer);
The parameters of method are adjustable, depending of the type of instrument used for titration.

Results and discussion

Titer determination and potentiometric determination of Ca was performed several times. Part of the results are presented:

- For titer determination an average value is used from three measured samples (m1 = 97.48 mg, m_2 = 97.54 mg and m_3 = 97.51 mg).

The volume consumed for titration was:
Blank (V_{titer}) = 0 mL
Sample 1 (V_{titer}) = 9.7420 mL
Sample 2 (V_{titer}) = 9.7209 mL
Sample 3 (V_{titer}) = 9.7144 mL

From the previous mentioned formula the calculated result for the titer value is:
Titer (Sample 1) = 1.0026
Titer (Sample 2) = 1.0025
Titer (Sample 2) = 1.0000
Average: 1.0017, RSD = 0.15%.

- The weights for the samples prepared are m_1 = 500.05 mg and m_2 = 500.34 mg.

The volume consumed for determination is:
Blank (V_{titer}) = 0 mL
Sample 1 (V_{titer}) = 4.1204 mL
Sample 2 (V_{titer}) = 4.1269 mL

With the formula for Ca content, the potentiometric method gave us results for the two samples prepared, 3.31% from the titration and 3.46% calculated on solvent free and anhydrous basis.

All calculations were performed using Tiamo software on the potentiometer.

Conclusion

From the results mentioned above and after performing the method multiple times, all the results were unified and according to the specification limits, which proves that the proposed method is accurate and suitable for determination of Ca content in pharmaceutical materials.

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