M1030-12-094

Selective and Sensitive Determination of Zinc in Various OTC Formulations as per USP <591>

Hari Narayanan[1], Shibu Paul[1], Michael Chang[2], Leonel M Santos[2]

Metrohm USA Inc[1], USP[2]

CONTACT INFORMATION: hari@metrohmusa.com

aaps PharmSci 360 ADVANCING PHARMACEUTICAL SCIENCES, CAREERS, AND COMMUNITY

PURPOSE

Zinc compounds are used as an active pharmaceutical ingredient in various over-the-counter (OTC) zinc containing formulations. Many of the zinc drug substances and drug products used to be tested for assay by manual titration methods. USP has embarked on a global initiative to modernize monographs across all of its compendia to include more selective and more sensitive methodologies. USP has updated the General Chapter <591> ZINC DETERMINATION to include a new ion chromatography (IC) method for zinc products. Individual zinc compounds in drug substances and drug products monographs are updated by USP as they become available. We tested the applicability of a new ion chromatography method for zinc oxide, zinc oxide powder and zinc sulfate ophthalmic solution using an alternative column, L91.

METHOD

Ion Chromatography is suitable for metal cation separation and detection. For zinc determination, two methods are possible. Separation as cationic species and detection by non-suppressed conductivity method, as shown in Figure 1, is very simple and straightforward.

Alternatively, zinc is separated as anionic dipicolinic acid complex using the L91 column and converted to Zn-4-(2-pyridylazo) resorcinol (PAR) complex, after post column reaction, and detected at 530 nm. The general instrumentation schematic is outlined in Figure 3.

A precise and pulse-free post column reagent (PCR) is critical in this method. The ratio of eluent to PCR volume is important to achieve a consistent response. Precise and pulse-free post column reagent delivery is achieved by patented Metrohm Dosino technology. PCR addition and rinsing the flow path with water after the sample queue can be automated with Dosino liquid handling. The instrumentation used in this study is shown in Figure 5.

Samples were prepared as per the individual monograph guidelines.

RESULT

Column equivalency was tested as per USP system suitability guidelines. The method was tested for zinc oxide, zinc oxide powder and zinc sulfate ophthalmic solution. The system suitability and sample analysis results are summarized in Table 1 below. As the individual monographs become available, they are posted in the Pharmaceutical Forum (PF). Figure 4 shows the methods in the Pharmaceutical Forum (PF) and the others that are expected soon.

Zinc Analysis in as per USP <591> By Ion Chromatography			
Parameters	**Metrohm**	**USP Monograph**	**Status**
Column	A Supp 10 250/4.0mm with A Supp 10 guard Column (L91)	L100	
Eluent	7.0mM Dipicolinic acid, 66.0mM Potassium hydroxide,5.6mM Potassium sulfate, and 74mM Formic acid (pH 4.2)	7.0mM Dipicolinic acid, 66.0mM Potassium hydroxide,5.6mM Potassium sulfate, and 74mM Formic acid (pH 4.2)	✓
Flow Rate	1.2mL/Min	1.2mL/Min	✓
PCR Reagent	0.5mM 4-(2-pyridylazo) resorcinol monosodium salt, 1.0M 2-methylaminoethanol, 0.50M ammonium hydroxide, and 0.3M sodium bicarbonate in water	0.5mM 4-(2-pyridylazo) resorcinol monosodium salt, 1.0M 2-methylaminoethanol, 0.50M ammonium hydroxide, and 0.3M sodium bicarbonate in water	✓
PCR Flow Rate	0.6mL/Min	0.6mL/Min	✓
Column Temperature	30°C	30°C	✓
Detection	Vis 530nm	Vis 530nm	✓
Injection Volume	10µL	10µL	✓
Standard: Used 1000ppm Zinc from ERA diluted with 0.2% HCl			
RSD from 6 replicates @ 15ppm Zinc	0.31%	NMT 2%	✓
Mean Tailing Factor from 6 replicates	1.437	NMT 2.0	✓
Sample: Clear Eyes, Medtech Products 0.25% ZnSO4.7H2O; Lot# X8479			
Mean Sample recovery: Duplicate Sample preparations	96%	95%-105%	✓
Sample: Johnson's Baby Powder; Zinc Oxide 10% (Lot# 33117RB)			
Mean Sample recovery: Duplicate Sample preparations	95%	90%-110%	✓
Sample:Alfa Aesar Zinc Oxide 99.99%			
Mean Sample recovery: Duplicate Sample preparations	98.9%	98%-102%	✓

Table 1: Result Summary

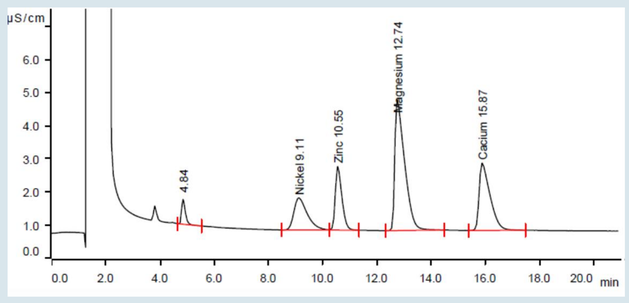

Fig 1: Zinc by Non-Suppressed Conductivity Detection; Column: L-76; Eluent: 2.5 mmol/L Nitric acid + 0.5 mmol/L Oxalic acid

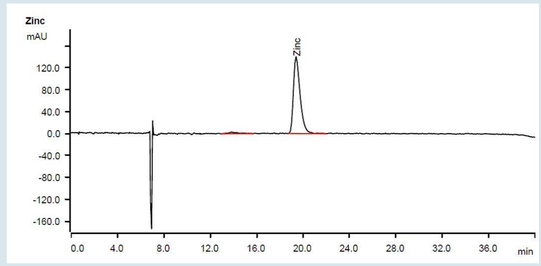

Fig 2: Zinc in zinc oxide sample as per USP <591>

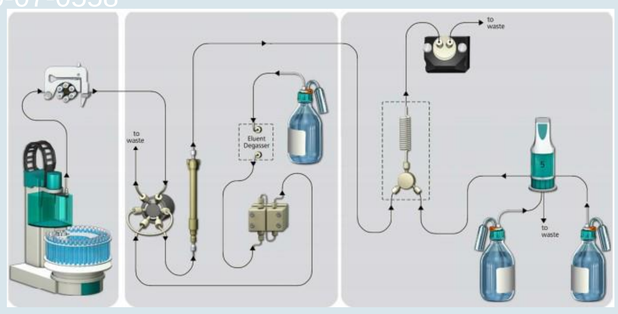

Fig 3: Ion Chromatography with PCR- UV-VIS detection, flow path

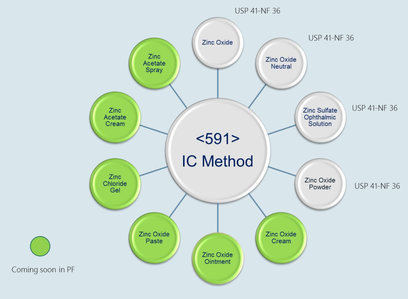

Fig.4: USP Monograph Modernization Progress

- Metrohm 940 Professional IC Vario
- Detection: Vis 530 nm
- Column Temperature: 30° C
- Flow Rate: 1.2 mL/min
- PCR Flow Rate: 0.6 mL/min
- Injection Volume: 10 µL
- Eluent : 4 mmol/L nitric acid - Isocratic separation
- Column: Metrosep A Supp 10-250/4.0, packing L91

Fig 5: Ion Chromatography instrument used for OTC assay

CONCLUSION

The new USP method for zinc as per <591> using Ion Chromatography is highly selective and sensitive. Selectivity is achieved by separation and further improved with PCR reaction. Sensitivity and the wide linear quantification limit make the new USP method ideal for QA/QC. Automated PCR delivery makes the overall method performance easy to validate.

8.000.6105EN

Metrohm USA Inc.