



Application Note AN-U-076

根据 USP 通用章 <591> 1)行化含量

USP monograph modernization utilizing ion chromatography as a valid analysis method

Zinc is an essential trace element which is used in different pharmaceuticals and supplements [1]. In the form of zinc oxide, zinc is an integral part of skin care creams, pastes, and supplements [2,3]. In order to meet the stringent quality standards for pharmaceutical products, manufacturers and laboratories must employ validated methods as from the United States Pharmacopeia and National Formulary (USP-NF). In the course of their modernization activities, USP-NF also updated the zinc monograph and replaced the existing identification procedure

with titration by ion chromatographic analyses. Ion chromatography (IC) qualified as a methodical approach for the zinc assay in General Chapter <591>, Zinc Determination [4]. The analysis involves separation of zinc using, e.g., L91 column material (Metrosep A Supp 10) followed by post-column reaction using 4-(2-pyridylazo)resorcinol (PAR) and subsequent detection at 530 nm. IC was validated according to USP procedures as a highly specific and accurate method to ensure product safety and quality.

SAMPLE AND SAMPLE PREPARATION

All analyses are performed with a solution of ultrapure zinc oxide. No additional sample

A sample stock solution is prepared by hydrolyzing 0.1868 g of ultrapure zinc oxide powder in 10 mL of 6 mol/L hydrochloric acid. This solution is made up to 100 mL in a volumetric flask with ultrapure water. The zinc concentration of this sample stock solution corresponds to 1500 g/mL. To prepare the final sample solution, the sample stock solution is diluted 1:100 with 0.2% (w/v) HCl to obtain a final concentration of 15 g/mL zinc.

The working standard solution is prepared from a certified 1000 g/mL zinc standard.

preparation is required unless stated in the individual USP monographs.

Samples and standard solutions were injected directly into the IC (**Figure 1**) using an 889 IC Sample Center – cool. Zinc is separated from all other cations using L91 column material (Metrosep A Supp 10 - 250/4.0 and Metrosep A Supp 10 Guard/4.0) applying the MetPac™ PDCA (pyridine-2,6-dicarboxylic acid) eluent (concentrate dilution 1:5) followed by post-column reaction (PCR) with MetPac™ PAR and subsequent detection at a wavelength of 530 nm.



Figure 1. Instrumental setup including a 930 Compact IC Flex with a 947 Professional UV/VIS Detector Vario, a 800 Dosino for PCR delivery and mixing, and an 889 IC Sample Center – cool. Cooling can prolong sample stability.

EXPERIMENTAL

The calibration was performed using a single 15 g/mL zinc standard injected six times. The sample

was analyzed in duplicate.

Table 1. Requirements for IC method as per USP General Chapter <591>.

Column with L91 packing	Metrosep A Supp 10 - 250/4.0
Eluent	MetPac™ PDCA concentrate (dilution 1:5)
Flow rate	1.2 mL/min
Temperature	30 °C
Injection volume	10 L
PCR reagent	PAR (0.12 g MetPac™ PAR reagent in 1000 mL MetPac™ PAR diluent)
PCR flow rate	0.6 mL/min
Detection	Vis: 530 nm after PCR

The IC assay for zinc content was validated according to USP General Chapter <591>, Zinc Determination [4]. Ultrapure zinc oxide was analyzed for its zinc content. The accuracy of the zinc determination was calculated as 99% (**Figure 2**).

All acceptance criteria were fulfilled, e.g., asymmetry (tailing factor) for the zinc peak was <2, or the relative standard deviation of the standard solutions was <0.73% (n = 6, USP requirement no more than (NMT) 0.73) (**Table 2**).

Table 2. Required acceptance criteria according to General Chapter <591>.

Parameter	Actual	USP requirement	Status
% RSD	0.582	NMT 0.73	Pass
Tailing factor	1.465	NMT 2.0	Pass
Result standard	98.9%	+/- 2%*	Pass
Results sample	99.2%	+/- 2%*	Pass

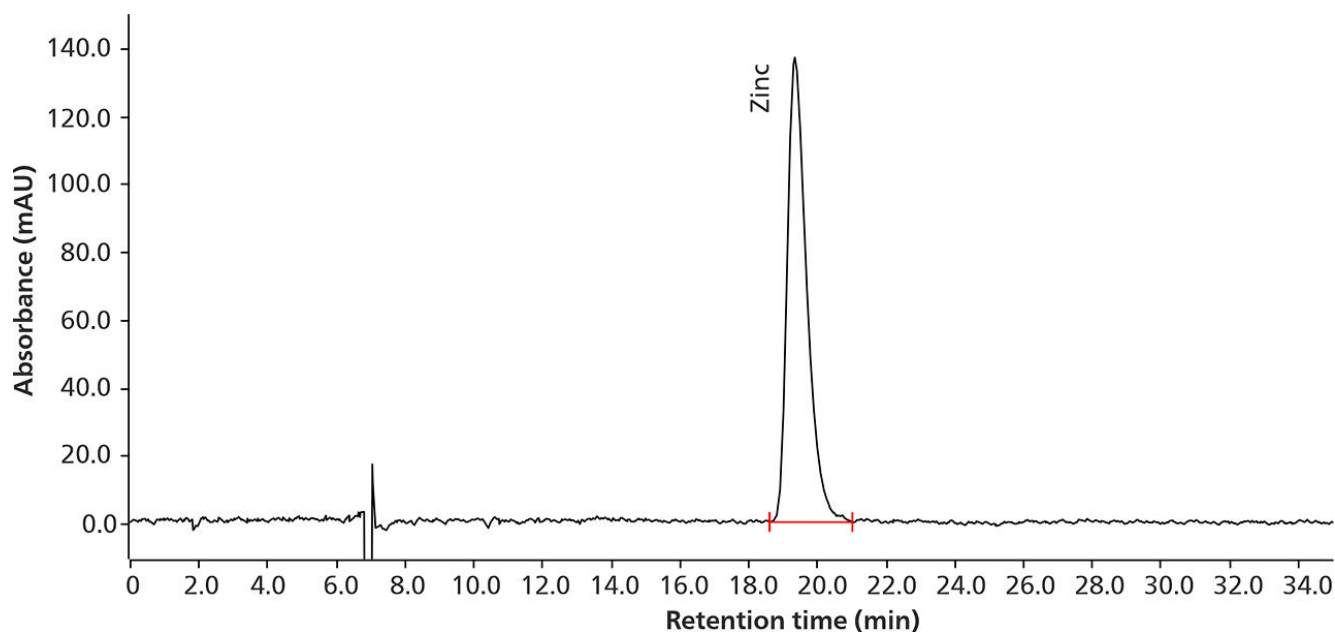


Figure 2. Chromatogram of zinc in a zinc oxide sample containing 14.865 µg/mL Zn (99.1% recovery of the nominal concentration).

CONCLUSION

Ion chromatography qualifies for the determination of zinc as per USP General Chapter <591>. Using the column material L91, zinc can be reliably determined in pharmaceuticals and other samples using IC with post-column reaction and UV detection. The high degree of automation possibilities for IC

systems from Metrohm (e.g., autosampler, Metrohm intelligent Partial Loop injection Technique, Inline Dilution, etc.) and the traceability of all steps during analysis make it a user-friendly, efficient, and valuable analytical technique for pharmaceutical quality control processes.

REFERENCES

1. Royal Society of Chemistry. *Zinc*. The Royal Society of Chemistry's interactive periodic table. <https://www.rsc.org/periodic-table/element/30/zinc>.
2. Juch, R. D.; Rufli, T.; Surber, C. Pastes: What Do They Contain? How Do They Work? *Dermatology* **1994**, 189 (4), 373–377. <https://doi.org/10.1159/000246882>.
3. Maier, T.; Korting, H. C. Sunscreens - Which and What For? *Skin Pharmacol Physiol* **2005**, 18 (6), 253–262. <https://doi.org/10.1159/000087606>.
4. U. S. Pharmacopeia/National Formulary. <591> Zinc Determination. In *General Chapter*; USP/NF, Rockville, MD, USA. https://doi.usp.org/USPNF/USPNF_M99350_05_01.html.

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CONFIGURATION



930 Compact IC Flex Oven/ChS/PP/Deg

930 Compact IC Flex Oven/ChS/PP/Deg 是智能型 Compact IC 器,有柱加炉、化学抑制和用于抑制器再生,以及内置的脱气装置。器可使用各分和方法。

典型的用范:

- 使用化学抑制和行子定
- 用子排斥色法和反向抑制定有机酸



889 IC Sample Center – cool

889 IC Sample Center – cool 自化解决方案也用于品量少的情况。与 889 IC Sample Center 相比,它具有冷却功能,因此是用于生物化学相域或定性差的品的最佳自器。



947 Professional UV/VIS Detector Vario SW

智能波 器,947 Professional UV/VIS Detector Vario SW,可紫外光或可光区域内的活性物行安全可靠定量操作。可一波。



Metrosep A Supp 10 - 250/4.0

Metrosep A Supp 10 - 250/4.0 分柱基于高容量聚乙/二乙共聚物,其粒大小 4.6 μm 。A-Supp-10 品系列中越 越的柱可提供越 越大的性和活性。特是在色分析的情况下,推荐使用 MSM-HC。在此分柱上也可修改各不同子分的温度、流速和淋洗液成分。

Metrosep A Supp 10 - 250/4.0 具有很高的容量。用于子度高的品、的分任以及用于分析各成分之度差很大的品。



Metrosep A Supp 10 Guard/4.0

Metrosep A Supp 10 Guard/4.0 Metrosep A Supp 10, «On Column Guard System» ,