

Status: Currently Official on 12-Feb-2025
Official Date: Official as of 01-May-2023
Document Type: General Chapter
DocId: GUID-86C3E3AA-BF1A-4CE4-9C06-8CA5B8BEE29E_4_en-US
DOI: https://doi.org/10.31003/USPNF_M1137_04_01
DOI Ref: 8jb4j

© 2025 USPC
Do not distribute

(345) ASSAY FOR CITRIC ACID/CITRATE AND PHOSPHATE

INTRODUCTION

The following ion chromatographic general procedure is provided for the determination of citric acid/citrate and phosphate in compendial articles, when specified in the individual monographs. See [Ion Chromatography \(1065\)](#) for discussion of the theory and principles of measurements using ion chromatography.

Change to read:

ASSAY

▲[NOTE—Use procedure A if the monograph does not specify a procedure.]▲ (USP 1-MAY-2023)

Change to read:

• PROCEDURE ▲A▲ (USP 1-MAY-2023)

Mobile phase: 20 mM sodium hydroxide or potassium hydroxide from an appropriate volume of carbonate-free sodium hydroxide or potassium hydroxide solution of known concentration and water (resistivity NLT 18 megohm-cm). Alternatively, *Mobile phase* can be generated electrolytically using an automatic eluent generator. Protect the *Mobile phase* from atmospheric carbon dioxide.

Standard solution 1 (for the assay of citric acid/citrate only): 20 µg/mL of citrate (C₆H₅O₇) in freshly prepared 1 mM sodium hydroxide from [USP Citric Acid RS](#)

Standard solution 2 (for the concomitant assay of citrate and phosphate): 20 µg/mL of citrate (C₆H₅O₇) and 12 µg/mL of phosphate (PO₄) in freshly prepared 1 mM sodium hydroxide from [USP Citric Acid RS](#) and monobasic sodium phosphate

Sample solution (for the assay of citric acid/citrate): Nominally 20 µg/mL of citrate in freshly prepared 1 mM sodium hydroxide, unless otherwise stated in the monograph

Sample solution (for the assay of phosphate): Nominally 12 µg/mL of phosphate in freshly prepared 1 mM sodium hydroxide, unless otherwise stated in the monograph

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: Conductivity with suppression

Columns

Analytical: 4-mm × 25-cm; 13-µm packing L61

Guard: 4-mm × 5-cm; 13-µm packing L61

Temperatures

Column: 30°

Detector: 35°

Suppressor: 4-mm membrane anionic autosuppressor or a suitable chemical suppression system

Flow rate: 2 mL/min

Injection volume: 10 µL

System suitability

Samples: *Standard solution 1* and/or *Standard solution 2*, as appropriate

[NOTE—The relative retention times for phosphate and citrate are 0.57 and 1.0, respectively.]

Suitability requirements

Tailing factor: NMT 2.0 for the citrate and/or phosphate peaks, as appropriate

Relative standard deviation: NMT 1.5% for six replicate injections for the citrate and/or phosphate peaks, as appropriate

Analysis

Samples: *Standard solution 1* and/or *Standard solution 2*, and *Sample solution*

Unless otherwise stated in the monograph, calculate the concentration of citrate or phosphate in the portion of the *Sample solution* taken:

$$\text{Result} = (r_U/r_S) \times C_S$$

r_U = peak response of citrate or phosphate from the *Sample solution*

r_s = peak response of citrate or phosphate from *Standard solution 1* or *Standard solution 2*

C_s = concentration of citrate or phosphate from *Standard solution 1* or *Standard solution 2* ($\mu\text{g/mL}$)

Add the following:

▲ **Procedure B**

Mobile phase, Standard solution 1, Standard solution 2, and Sample solution(s): Prepare as directed in *Procedure A*.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode, Detector, Temperatures, Suppressor, and Injection volume: Proceed as directed in *Procedure A*.

Columns

Guard: 4-mm \times 5-cm; 10- μm packing [L21](#)

Analytical: 4.6-mm \times 25-cm; 9- μm packing [L46](#)

Flow rate: 1 mL/min

Run time: 15 min

System suitability

Samples: *Standard solution 1* and/or *Standard solution 2*, as appropriate

[NOTE—The relative retention times for phosphate and citrate are 0.65 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 6.5 between phosphate and citrate, *Standard solution 2*

Tailing factor: NMT 1.5 for citrate and/or phosphate, as appropriate

Relative standard deviation: NMT 1.5% for 6 replicate injections for citrate and/or phosphate, as appropriate

Analysis: Proceed as directed in *Procedure A*. ▲ (USP 1-May-2023)

ADDITIONAL REQUIREMENTS

• **USP REFERENCE STANDARDS (11)**

[USP Citric Acid RS](#)

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
<345> ASSAY FOR CITRIC ACID/CITRATE AND PHOSPHATE	Margareth R.C. Marques Principal Scientific Liaison	GCCA2020 General Chapters - Chemical Analysis 2020

Most Recently Appeared In:

Pharmacopeial Forum: Volume No. 47(6)

Current DocID: [GUID-86C3E3AA-BF1A-4CE4-9C06-8CA5B8BEE29E_4_en-US](#)

DOI: https://doi.org/10.31003/USPNF_M1137_04_01

DOI ref: [8jb4j](#)