

HANDBOOK OF  
**PHARMACEUTICAL**  
**EXCIPIENTS**

THIRD EDITION



**APhA**  
American  
Pharmaceutical  
Association



EDITED BY

**ARTHUR H. KIBBE**

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# Handbook of PHARMACEUTICAL EXCIPIENTS

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Third Edition

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# Citric Acid Monohydrate

## 1. Nonproprietary Names

BP: Citric acid monohydrate  
 JP: Citric acid  
 PhEur: Acidum citricum monohydricum  
 USP: Citric acid

## 2. Synonyms

2-Hydroxypropane-1,2,3-tricarboxylic acid monohydrate.

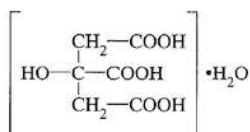
## 3. Chemical Name and CAS Registry Number

2-Hydroxy-1,2,3-propanetricarboxylic acid monohydrate  
 [5949-29-1]

## 4. Empirical Formula Molecular Weight

$C_6H_8O_7 \cdot H_2O$  210.14

## 5. Structural Formula



## 6. Functional Category

Acidifying agent; antioxidant; buffering agent; chelating agent; flavor enhancer.

## 7. Applications in Pharmaceutical Formulation or Technology

Citric acid, as either the monohydrate or anhydrous material, is widely used in pharmaceutical formulations and food products primarily to adjust the pH of solutions. Citric acid monohydrate is used in the preparation of effervescent granules while anhydrous citric acid is widely used in the preparation of effervescent tablets.<sup>(1)</sup>

In food products, citric acid is used as a flavor enhancer, for its tart, acid taste. Citric acid monohydrate is also used as a sequestering agent and antioxidant synergist. It is a component of anticoagulant citrate solutions. Therapeutically, preparations containing citric acid have been used to dissolve renal calculi.

| Use                                     | Concentration (%) |
|---|-------------------|
| Buffer solutions                        | 0.1-2.0           |
| Flavor enhancer for liquid formulations | 0.3-2.0           |
| Sequestering agent                      | 0.3-2.0           |

## 8. Description

Citric acid monohydrate occurs as colorless or translucent crystals, or as a white crystalline, efflorescent powder. It is odorless and has a strong acidic taste. Crystal structure is orthorhombic.

## 9. Pharmacopeial Specifications

| Test                            | JP       | PhEur     | USP         |
|---------------------------------|----------|-----------|-------------|
| Identification                  | +        | +         | +           |
| Clarity and color of solution   | —        | +         | —           |
| Water                           |          |           |             |
| (hydrous form)                  | —        | 7.5-9.0%  | ≤ 8.8%      |
| (anhydrous form)                | —        | ≤ 1.0%    | ≤ 0.5%      |
| Bacterial endotoxins            | —        | +         | —           |
| Residue on ignition             | —        | —         | ≤ 0.05      |
| Sulfated ash                    | ≤ 0.1%   | —         | ≤ 0.1%      |
| Barium                          | —        | +         | —           |
| Calcium                         | +        | ≤ 200 ppm | —           |
| Aluminum                        | —        | +         | —           |
| Oxalate                         | +        | ≤ 350 ppm | +           |
| Sulfate                         | ≤ 0.048% | ≤ 150 ppm | +           |
| Arsenic                         | ≤ 1 ppm  | —         | ≤ 3 ppm     |
| Heavy metals                    | ≤ 10 ppm | ≤ 10 ppm  | ≤ 0.001%    |
| Iron                            | —        | ≤ 50 ppm  | —           |
| Chloride                        | —        | ≤ 50 ppm  | —           |
| Readily carbonizable substances | +        | +         | +           |
| Polycyclic aromatic hydrocarbon | +        | —         | —           |
| Organic volatile impurities     | —        | —         | +           |
| Assay (anhydrous basis)         | ≥ 99.5%  | 99.5-101% | 99.5-100.5% |

## 10. Typical Properties

Acidity/alkalinity:

pH = 2.2 (1% w/v aqueous solution)

Dissociation constants:

pK<sub>a1</sub>: 3.128 at 25°C;

pK<sub>a2</sub>: 4.761 at 25°C;

pK<sub>a3</sub>: 6.396 at 25°C.

Density: 1.542 g/cm<sup>3</sup>

Heat of combustion:

-1972 kJ/mol (-471.4 kcal/mol)

Heat of solution:

-16.3 kJ/mol (-3.9 kcal/mol) at 25°C

**Hygroscopicity:** at relative humidities less than about 65% citric acid monohydrate effloresces at 25°C, the anhydrous acid being formed at relative humidities less than about 40%. At relative humidities between about 65-75%, citric acid monohydrate absorbs insignificant amounts of moisture but under more humid conditions substantial amounts of water are absorbed.

**Melting point:** ~ 100°C (softens at 75°C)

**Particle size distribution:** various grades of citric acid monohydrate with different particle sizes are commercially available.

**Solubility:** soluble 1 in 1.5 parts of ethanol (95%) and 1 in less than 1 part of water; sparingly soluble in ether.

**Viscosity (dynamic):** 6.5 mPa s (6.5 cP) for a 50% w/v aqueous solution at 25°C

See also Section 18.

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