

Phosphoric Acid

1 Nonproprietary Names

BP: Phosphoric acid
PhEur: Acidum phosphoricum concentratum
USPNF: Phosphoric acid
See also Section 17.

2 Synonyms

Acid fosforico; acide phosphorique; E338; hydrogen phosphate; syrupy phosphoric acid.

3 Chemical Name and CAS Registry Number

Orthophosphoric acid [7664-38-2]

4 Empirical Formula Molecular Weight

H_3PO_4 98.00

5 Structural Formula

H_3PO_4

6 Functional Category

Acidifying agent.

7 Applications in Pharmaceutical Formulations or Technology

Phosphoric acid is widely used as an acidifying and buffering agent in a variety of pharmaceutical formulations. It is also widely used in food preparations as an acidulant, flavor, and synergistic antioxidant (0.001–0.005%) and sequestrant.

Therapeutically, dilute phosphoric acid has been used well-diluted in preparations used in the treatment of nausea and vomiting. Phosphoric acid 35% gel has also been used in dentistry to etch tooth enamel.

8 Description

Concentrated phosphoric acid occurs as a colorless, odorless, syrupy liquid.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for phosphoric acid.

	PhEur 2002	USPNF 20
Identification	+	+
Characters	+	—
Appearance of solution	+	—
Relative density	≈ 1.7	—
Sulfate	≤ 100 ppm	+
Chloride	≤ 50 ppm	—
Heavy metals	≤ 10 ppm	$\leq 0.001\%$
Substances precipitated with ammonia	+	—
Arsenic	≤ 2 ppm	—
Iron	≤ 50 ppm	—
Alkali phosphates	—	+
Limit of nitrate	—	+
Phosphorous or hypophosphorous acid	+	+
Assay (of H_3PO_4)	84.0–90.0%	85.0–88.0%

10 Typical Properties

Acidity/alkalinity: pH = 1.6 (1% w/w aqueous solution)

Boiling point: 117.87 °C

Dissociation constant:

$\text{p}K_{\text{a}1} = 2.15$

$\text{p}K_{\text{a}2} = 7.09$

$\text{p}K_{\text{a}3} = 12.32$

Melting point: 42.35 °C

Refractive index:

$n_{\text{D}}^{17.5} = 1.35846$ (30% w/w aqueous solution)

$n_{\text{D}}^{17.5} = 1.35032$ (20% w/w aqueous solution)

$n_{\text{D}}^{17.5} = 1.3423$ (10% w/w aqueous solution)

Solubility: miscible with alcohol and water with the evolution of heat.

Specific gravity:

1.874 (100% w/w) at 25 °C;

1.6850 (85% w/w aqueous solution) at 25 °C;

1.3334 (50% w/w aqueous solution) at 25 °C;

1.0523 (10% w/w aqueous solution) at 25 °C.

11 Stability and Storage Conditions

When stored at a low temperature, phosphoric acid may solidify, forming a mass of colorless crystals, comprised of the hemihydrate, which melt at 28 °C. Phosphoric acid should be stored in an airtight container in a cool, dry place. Stainless steel containers may be used.

12 Incompatibilities

Phosphoric acid is a strong acid and reacts with alkaline substances. Mixtures with nitromethane are explosive.

13 Method of Manufacture

The majority of phosphoric acid is made by digesting phosphate rock (essentially tricalcium phosphate) with sulfuric acid; the phosphoric acid is then separated by slurry filtration. Purification is achieved via chemical precipitation, solvent extraction, crystallization, or ion exchange.

14 Safety

In the concentrated form, phosphoric acid is an extremely corrosive and harmful acid. However, when used in pharmaceutical formulations it is usually very diluted and is generally regarded as an essentially nontoxic and nonirritant material.

The lowest lethal oral dose of concentrated phosphoric acid in humans is reported to be 1286 $\mu\text{L/kg}$.⁽¹⁾

LD₅₀ (rabbit, skin): 2.74 g/kg⁽¹⁾

LD₅₀ (rat, oral): 1.53 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Phosphoric acid is corrosive and can cause burns on contact with the skin, eyes and mucous membranes; contact should be avoided. Splashes should be washed with copious quantities of water. Protective clothing, gloves and eye protection are recommended.

Phosphoric acid is also irritant on inhalation. In the UK, the occupational exposure limit for phosphoric acid is 8 mg/m³ long-term (8-hour TWA) and 2 mg/m³ short-term (15-minutes).⁽²⁾

Phosphoric acid emits toxic fumes on heating.

16 Regulatory Status

GRAS listed. Accepted as a food additive in Europe. Included in the FDA Inactive Ingredients Guide (infusions, injections, oral solutions, topical creams, lotions, ointments and solutions, and vaginal preparations). Included in nonparenteral and parenteral medicines licensed in the UK.

17 Related Substances

Dilute phosphoric acid.

Dilute phosphoric acid

Synonyms: acidum phosphoricum dilutum; diluted phosphoric acid.

Comments: the PhEur 2002 states that dilute phosphoric acid contains 9.5–10.5% w/w H₃PO₄ and may be prepared by mixing phosphoric acid 115 g with 885 g of water. The USP NF 20 contains a monograph for diluted phosphoric acid and states that it contains 9.5–10.5% w/v H₃PO₄ and may be prepared by mixing phosphoric acid 69 mL with water to 1000 mL.

18 Comments

The EINECS number for phosphoric acid is 231-633-2.

In the UK, a 1 in 330 aqueous solution of phosphoric acid is approved as a disinfectant for foot-and-mouth disease.

19 Specific References

- 1 Lewis RJ, ed. *Sax's Dangerous Properties of Industrial Materials*, 10th edn. New York: Wiley, 2000: 2946.
- 2 Health and Safety Executive. *EH40/2002: Occupational Exposure Limits 2002*. Sudbury: Health and Safety Executive, 2002.

20 General References

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21 Author

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22 Date of Revision

30 May 2002.