Malic Acid

1 Nonproprietary Names

USPNF: Malic acid

2 Synonyms

Apple acid; E296; 2-hydroxy-1,4-butanedioic acid; hydroxybutanedioic acid; 1-hydroxy-1,2-ethanedicarboxylic acid; hydroxysuccinic acid; 2-hydroxysuccinic acid; DL-malic acid.

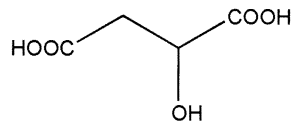
3 Chemical Name and CAS Registry Number

Hydroxybutanedioic acid [6915-15-7]
(RS)-(±)-Hydroxybutanedioic acid [617-48-1]

4 Empirical Formula and Molecular Weight

Empirical Formula	Molecular Weight
$C_4H_6O_5$	134.09

5 Structural Formula



6 Functional Category

Acidulant; antioxidant; chelating and buffering agent; flavoring agent; therapeutic agent.

7 Applications in Pharmaceutical Formulation or Technology

Malic acid is used in pharmaceutical formulations as a general-purpose acidulant. It possesses a slight apple flavor and is used as a flavoring agent to mask bitter tastes and provide tartness. Malic acid is also used as an alternative to citric acid in effervescent powders, mouthwashes, and tooth-cleaning tablets.

In addition, malic acid has chelating and antioxidant properties. It may be used with butylated hydroxytoluene as a synergist in order to retard oxidation in vegetable oils. In food products it may be used in concentrations up to 420 ppm.

Therapeutically, malic acid has been used topically in combination with benzoic acid and salicylic acid to treat burns, ulcers, and wounds. It has also been used orally and parenterally, either intravenously or intramuscularly, in the treatment of liver disorders, and as a sialagogue.[1]

8 Description

White or nearly white, crystalline powder or granules having a slight odor and a strongly acidic taste. It is hygroscopic. The synthetic material produced commercially in Europe and the USA is a racemic mixture, whereas the naturally occurring material found in apples and many other fruits and plants is levorotatory.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for malic acid.

Test	USPNF 20
Identification	+
Residue on ignition	⩽0.1%
Water-insoluble substances	⩽0.1%
Heavy metals	⩽0.002%
Fumaric acid	⩽1.0%
Maleic acid	⩽0.05%
Organic volatile impurities	+
Assay	99.0–100.5%

10 Typical Properties

Data shown below are for the racemate. *See* Section 17 for other data for the D- and L- forms.

Acidity/alkalinity: pH = 2.35 (1% w/v aqueous solution at 25 °C)

Boiling point: 150 °C (with decomposition)

Density (bulk): 0.81 g/cm^3

Density (tapped): 0.92 g/cm^3

Dissociation constant:

pK_{a1} = 3.40 at 25 °C

pK_{a2} = 5.05 at 25 °C

Melting point: 31–132 °C

Solubility: freely soluble in ethanol (95%) and water but practically insoluble in benzene. A saturated aqueous solution contains about 56% malic acid at 20 °C. *See* Table II.

Table II: Solubility of malic acid.

Solvent	Solubility at 20 °C unless otherwise stated
Acetone	1 in 5.6
Diethyl ether	1 in 119
Ethanol (95%)	1 in 2.6
Methanol	1 in 1.2
Propylene glycol	1 in 1.9
Water	1 in 1.5–2.0

Specific gravity:

1.601 at 20 °C

1.250 (saturated aqueous solution at 25 °C)

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

11 Stability and Storage Conditions

Malic acid is stable at temperatures up to 150 °C. At temperatures above 150 °C it begins to lose water very slowly to yield fumaric acid; complete decomposition occurs at about 180 °C to give fumaric acid and maleic anhydride.

Malic acid is readily degraded by many aerobic and anaerobic microorganisms. Conditions of high humidity and elevated temperatures should be avoided to prevent caking.

The effects of grinding and humidity on malic acid have also been investigated.[2]

The bulk material should be stored in a well-closed container, in a cool, dry place.

12 Incompatibilities

Malic acid can react with oxidizing materials. Aqueous solutions are mildly corrosive to carbon steels.

13 Method of Manufacture

Malic acid is manufactured by hydrating maleic and fumaric acids in the presence of suitable catalysts. The malic acid formed is then separated from the equilibrium product mixture.

14 Safety

Malic acid is used in oral, topical, and parenteral pharmaceutical formulations in addition to food products, and is generally regarded as a relatively nontoxic and nonirritant material. However, concentrated solutions may be irritant.

LD_{50} (rat, oral): 1.6 g/kg[3]
LD_{50} (rat, IP): 0.1 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Malic acid, and concentrated malic acid solutions may be irritant to the skin, eyes, and mucous membranes. Gloves and eye protection are recommended.

16 Regulatory Status

GRAS listed. Both the racemic mixture and the levorotatory isomer are accepted as food additives in Europe. The DL- and L- forms are included in the FDA Inactive Ingredients Guide (oral and rectal preparations). Included in nonparenteral and parenteral medicines licensed in the UK.

17 Related Substances

Citric acid; fumaric acid; D-malic acid; L-malic acid; tartaric acid.

D-Malic acid

Empirical formula: $C_4H_6O_5$
Molecular weight: 134.09
CAS number: [636-61-3]
Synonyms: (*R*)-(+)-hydroxybutanedioic acid; D-(+)-malic acid.
Melting point: 99–101 °C
Specific rotation $[\alpha]_D^{20}$: +5.2 ° (in acetone at 18 °C).

L-Malic acid

Empirical formula: $C_4H_6O_5$
Molecular weight: 134.09
CAS number: [97-67-6]
Synonyms: apple acid; (*S*)-(–)-hydroxybutanedioic acid; L-(–)-malic acid.
Boiling point: ≈140 °C (with decomposition)
Melting point: 99–100 °C
Solubility: practically insoluble in benzene. *See also* Table III.

Table III: Solubility of L-malic acid

Solvent	Solubility at 20 °C
Acetone	1 in 1.6
Diethyl ether	1 in 37
Dioxane	1 in 1.3
Ethanol	1 in 1.2
Methanol	1 in 0.51
Water	1 in 2.8

Specific gravity: 1.595 at 20 °C
Specific rotation $[\alpha]_D^{20}$: −5.7 ° (in acetone at 18 °C)

18 Comments

The EINECS number for malic acid is 202-601-5.

19 Specific References

1 Sweetman SC, ed. *Martindale: The Complete Drug Reference*, 33rd edn. London: Pharmaceutical Press, 2002: 1631.
2 Piyarom S, Yonemochi E, Oguchi T, Yamamoto K. Effects of grinding and humidification on the transformation of conglomerate to racemic compound in optically active drugs. *J Pharm Pharmacol* 1997; **49**: 384–389.
3 Lewis RJ, ed. *Sax's Dangerous Properties of Industrial Materials*, 10th edn. New York: Wiley, 2000: 2272.

20 General References

Anonymous. Malic and fumaric acids. *Manuf Chem Aerosol News* 1964; 35(12): 56–59.
Berger SE. In: *Kirk-Othmer Encyclopedia of Chemical Technology*, vol. 13, 3rd edn. New York: Wiley-Interscience, 1981: 103.

21 Author

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22 Date of Revision

21 May 2002.