

# Trehalose

## 1 Nonproprietary Names

None adopted.

## 2 Synonyms

( $\alpha$ -D-Glucosido)- $\alpha$ -D-glucoside; mycose; natural trehalose;  $\alpha,\alpha$ -trehalose; trehalose dihydrate.

## 3 Chemical Name and CAS Registry Number

$\alpha$ -D-Glucopyranosyl- $\alpha$ -D-glucopyranoside anhydrous [99-20-7]  
 $\alpha$ -D-Glucopyranosyl- $\alpha$ -D-glucopyranoside dihydrate  
[6138-23-4]

See also Section 17.

## 4 Empirical Formula

$C_{12}H_{22}O_{11}$

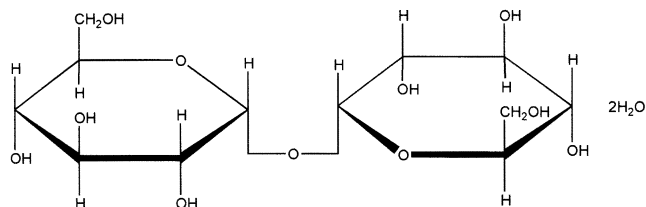
$C_{12}H_{22}O_{11}\cdot 2H_2O$

## Molecular Weight

342.31 (anhydrous)

378.33 (dihydrate)

## 5 Structural Formula



$\alpha,\alpha$ -Trehalose dihydrate

## 6 Functional Category

Coloring adjuvant; flavor enhancer; freeze-drying excipient; humectant; stabilizing agent; sweetening agent; tablet diluent; thickening agent.

## 7 Applications in Pharmaceutical Formulation or Technology

Trehalose is used for the lyoprotection of therapeutic proteins, particularly for parenteral administration. Other pharmaceutically relevant applications include use as an excipient for diagnostic assay tablets,<sup>(1)</sup> for stabilization during the freeze-thaw and lyophilization of liposomes,<sup>(2)</sup> and for stabilization of blood cells,<sup>(3)</sup> cosmetics,<sup>(4)</sup> and monoclonal antibodies.<sup>(5)</sup> Trehalose may also be used in formulations for topical application.<sup>(6)</sup>

## 8 Description

Trehalose occurs as virtually odorless, white or almost white-crystals with a sweet taste (approximately 45% of the sweetness of sucrose).

## 9 Pharmacopeial Specifications

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## 10 Typical Properties

**Acidity/alkalinity:** pH = 4.5–6.5 (30% w/v aqueous solution)

**Melting point:** 97°C (for the dihydrate)

**Moisture content:** 9.5% (for the dihydrate)

**Solubility:** soluble in water; very slightly soluble in ethanol (95%); practically insoluble in ether.

**Specific rotation** $[\alpha]_D^{20}$ : +179.7° (5% w/v aqueous solution)

See also Section 18.

## 11 Stability and Storage Conditions

Trehalose is a relatively stable material. At 60°C for 5 hours it loses not more than 1.5% w/w of water (the dihydrate water of crystallization is retained). Open stored powder may liquefy at high relative humidity ( $\geq 90\%$ ).

Trehalose should be stored in a cool, dry place in a well-sealed container.

## 12 Incompatibilities

Trehalose is incompatible with strong oxidizing agents, especially in the presence of heat.

## 13 Method of Manufacture

Trehalose is prepared from liquefied starch by a multistep enzymatic process.<sup>(7)</sup> The commercial product is the dihydrate.

## 14 Safety

Trehalose is used in cosmetics, foods, and parenteral and nonparenteral pharmaceutical formulations. It is generally regarded as a relatively nontoxic and nonirritant material when used as an excipient.

In the gut, trehalose is rapidly metabolized to glucose by the specific enzyme trehalase. A small minority of the population exhibits a primary (hereditary) or secondary (acquired) trehalase deficiency and thus may experience intestinal discomfort after ingestion of excessive amounts of trehalose owing to the osmotic activity of undigested trehalose in the gut. However, smaller amounts of trehalose are tolerated by such individuals without any symptoms.<sup>(7)</sup>

Trehalose is reported to have substantially less cariogenic potential than sucrose.

LD<sub>50</sub> (dog, IV): >1 g/kg

LD<sub>50</sub> (dog, oral): >5 g/kg

LD<sub>50</sub> (mouse, IV): >1 g/kg

LD<sub>50</sub> (mouse, oral): >5 g/kg

LD<sub>50</sub> (rat, IV): >1 g/kg

LD<sub>50</sub> (rat, oral): >5 g/kg

## 15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Eye protection and gloves are recommended.

## 16 Regulatory Status

GRAS listed. In the UK trehalose may be used in certain food applications. Included in parenteral and nonparenteral investigational formulations.

## 17 Related Substances

Isotrehalose; neotrehalose.

### Isotrehalose

CAS number: [499-23-0]

Synonyms:  $\beta,\beta$ -trehalose.

### Neotrehalose

CAS number: [585-91-1]

Synonyms:  $\alpha,\beta$ -trehalose.

## 18 Comments

$\alpha,\alpha$ -Trehalose is the only naturally occurring isomer of trehalose and occurs as the dihydrate. However,  $\alpha,\beta$ -trehalose (neotrehalose) and  $\beta,\beta$ -trehalose (isotrehalose) have been synthesized and are also available commercially. *See also* Section 17.

Trehalose is a nonreducing sugar and therefore does not react with amino acids or proteins as a part of Maillard browning. It is relatively stable under low-pH conditions compared to other disaccharides.

It should be noted that although trehalose dihydrate is quoted to have a melting point of 97°C, the true nature of this melting process has been the subject of debate in the literature,<sup>(8,9)</sup> including the transformation of the dihydrate into the anhydrous form. Anhydrous crystalline trehalose has been reported to melt at 203°C,<sup>(10)</sup> although higher values (215°C) have also been quoted in the literature.<sup>(11)</sup>

The glass transition temperature of trehalose is reported to be approximately 120°C (anhydrous amorphous phase).<sup>(12)</sup>

The EINECS number for trehalose is 202-739-6.

## 19 Specific References

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## 20 General References

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## 22 Date of Revision

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