Neohesperidin Dihydrochalcone

1 Nonproprietary Names

BP: Neohesperidin Dihydrochalcone

PhEur: Neohesperidin Dihydrochalcone

2 Synonyms

Citrosa; 1-[4-[[2-*O*-6-deoxy-α-L-mannopyranosyl)-β-D-glycopyranosyl]oxy]-2,6-dihydroxyphenyl]-3-(3-hydroxy-4-methoxyphenyl); 3,5-dihydroxy-4-(3-hydroxy-4-methoxyhydrocinnamoyl)phenyl-2-*O*-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranoside; 3,5-dihydroxy-4-[3-(3-hydroxy-4-methoxyphenyl)propionyl]phenyl-2-*O*-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranoside; E959; neohesperidin DC; neohesperidin DHC; neohesperidin dihydrochalconum; neohesperidine dihydrochalcone; NHDC; 1-propanone; *Sukor*.

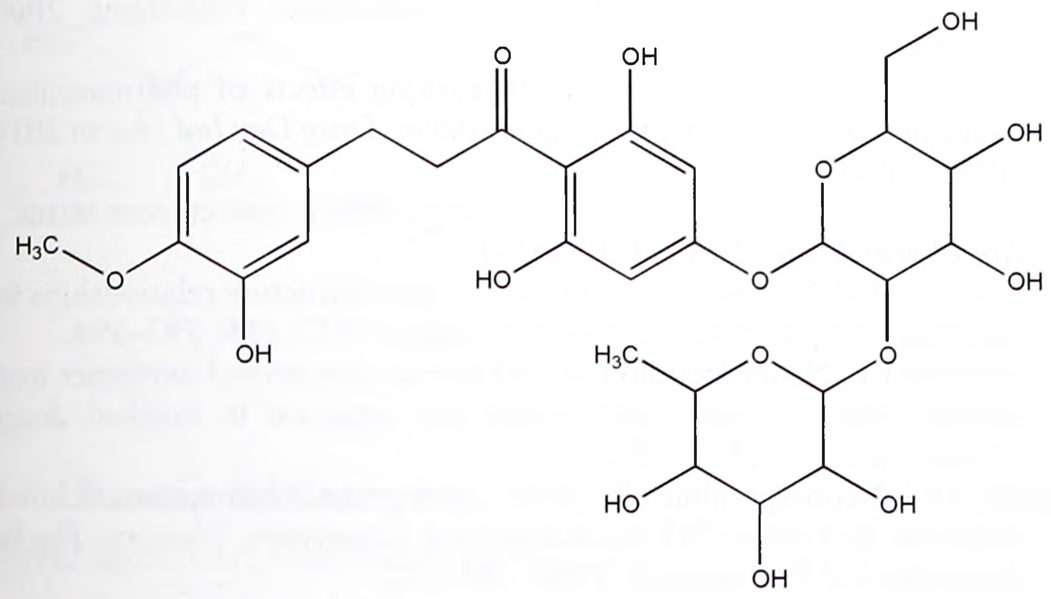
3 Chemical Name and CAS Registry Number

1-[4-[[2-*O*-(6-Deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-2,6-dihydroxyphenyl]-3-(3-hydroxy-4-methoxyphenyl)propan-1-one [20702-77-6]

4 Empirical Formula and Molecular Weight

$C_{28}H_{36}O_{15}$ 612.58

5 Structural Formula



6 Functional Category

Flavor enhancer; sweetening agent.

7 Applications in Pharmaceutical Formulation or Technology

Neohesperidin dihydrochalcone is a synthetic intense sweetening agent approximately 1000–1500 times sweeter than sucrose and 20 times sweeter than saccharin. Structurally it is an analogue of neohesperidin, a flavanone that occurs naturally in Seville oranges (*Citrus aurantium*).

Neohesperidin dihydrochalcone is used in pharmaceutical and food applications as a sweetening agent and flavor enhancer. The sweetness profile is characterized by a lingering sweet/menthol-like aftertaste.[1] The typical level used in foods is 1–5 ppm although much higher levels may be used in certain applications such as chewing gum. Synergistic effects occur with other intense and bulk sweeteners such as acesulfame K, aspartame, polyols, and saccharin.[2]

In pharmaceutical applications, neohesperidin dihydrochalcone is useful in masking the unpleasant bitter taste of a number of drugs such as antacids, antibiotics, and vitamins. In antacid preparations, levels of 10–30 ppm result in improved palatability.

8 Description

Neohesperidin dihydrochalcone occurs as a white or yellowish-white powder with an intensely sweet taste.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for neohesperidin dihydrochalcone.

Test	PhEur 9.2
Identification	+
Characters	+
Appearance of solution	+
Related substances	+
Water	≤12.0%
Sulfated ash	≤0.2%
Assay (anhydrous substance)	96.0–101.0%

10 Typical Properties

Hygroscopicity Slightly hygroscopic; absorbs up to 15% of water.
Melting point 156–158°C
Solubility *see* Table II.

Table II: Solubility of neohesperidin dihydrochalcone.

Solvent	Solubility at 25°C unless otherwise stated
Dichloromethane	Practically insoluble
Dimethyl sulfoxide	Freely soluble
Methanol	Soluble
Water	1 in 2000 at 22°C 1 in 1.54 at 80°C

11 Stability and Storage Conditions

Neohesperidin dihydrochalcone is stable for over three years when stored at room temperature.[1]

Accelerated stability studies on aqueous solutions stored at 30–60°C and pH 1–7 for 140 days indicate that neohesperidin dihydrochalcone solutions are likely to be stable for 12 months at room temperature and pH 2–6.[3] Solutions formulated with some or all of the water replaced by solvents with a lower dielectric constant are reported to have longer shelf-lives.[4]

The bulk material should be stored in a cool, dry place protected from light.

12 Incompatibilities

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13 Method of Manufacture

Neohesperidin dihydrochalcone is synthesized commercially from either of the bitter-flavanones neohesperidin or naringin by catalytic