

The therapeutic use of sodium propionate in topical antifungal preparations has largely been superseded by a new generation of antifungal drugs.

A specification for sodium propionate is contained in the Food Chemicals Codex (FCC).⁽⁶⁾

The EINECS number for sodium propionate is 205-290-4. The PubChem Compound ID (CID) for sodium propionate is 23663426.

19 Specific References

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21 Author

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22 Date of Revision

5 February 2009.

Sodium Starch Glycolate

1 Nonproprietary Names

BP: Sodium Starch Glycolate

PhEur: Sodium Starch Glycolate

USP-NF: Sodium Starch Glycolate

2 Synonyms

Carboxymethyl starch, sodium salt; carboxymethylamylum natrium; *Explosol*; *Explotab*; *Glycolys*; *Primojel*; starch carboxymethyl ether, sodium salt; *Tablo*; *Vivastar P*.

3 Chemical Name and CAS Registry Number

Sodium carboxymethyl starch [9063-38-1]

4 Empirical Formula and Molecular Weight

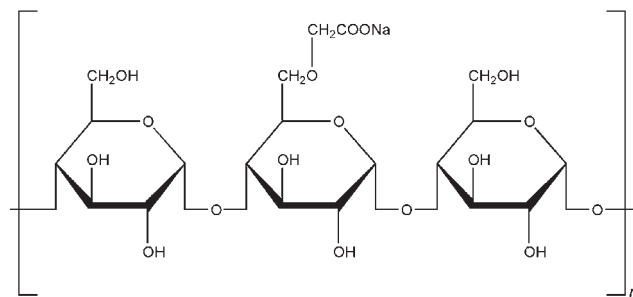
The USP32–NF27 describes two types of sodium starch glycolate, Type A and Type B, and states that sodium starch glycolate is the sodium salt of a carboxymethyl ether of starch or of a crosslinked carboxymethyl ether of starch.

The PhEur 6.0 describes three types of material: Type A and Type B are described as the sodium salt of a crosslinked partly O-carboxymethylated potato starch. Type C is described as the sodium salt of a partly O-carboxymethylated starch, crosslinked by physical dehydration. Types A, B, and C are differentiated by their pH, sodium, and sodium chloride content.

The PhEur and USP–NF monographs have been harmonized for Type A and Type B variants.

Sodium starch glycolate may be characterized by the degree of substitution and crosslinking. The molecular weight is typically 5×10^5 – 1×10^6 .

5 Structural Formula



6 Functional Category

Tablet and capsule disintegrant.

7 Applications in Pharmaceutical Formulation or Technology

Sodium starch glycolate is widely used in oral pharmaceuticals as a disintegrant in capsule^(1–6) and tablet formulations.^(7–10) It is commonly used in tablets prepared by either direct-compression^(11–13) or wet-granulation processes.^(14–16) The usual concentration employed in a formulation is between 2% and 8%, with the optimum concentration about 4%, although in many cases 2% is sufficient. Disintegration occurs by rapid uptake of water followed by rapid and enormous swelling.^(17–20)

Although the effectiveness of many disintegrants is affected by the presence of hydrophobic excipients such as lubricants, the disintegrant efficiency of sodium starch glycolate is unimpaired. Increasing the tablet compression pressure also appears to have no effect on disintegration time.^(10–12)

Sodium starch glycolate has also been investigated for use as a suspending vehicle.⁽²¹⁾

8 Description

Sodium starch glycolate is a white or almost white free-flowing very hygroscopic powder. The PhEur 6.0 states that when examined under a microscope it is seen to consist of: granules, irregularly shaped, ovoid or pear-shaped, 30–100 μm in size, or rounded, 10–35 μm in size; compound granules consisting of 2–4 components occur occasionally; the granules have an eccentric hilum and clearly visible concentric striations. Between crossed nicol prisms, the granules show a distinct black cross intersecting at the hilum; small crystals are visible at the surface of the granules. The granules show considerable swelling in contact with water.

9 Pharmacopeial Specifications

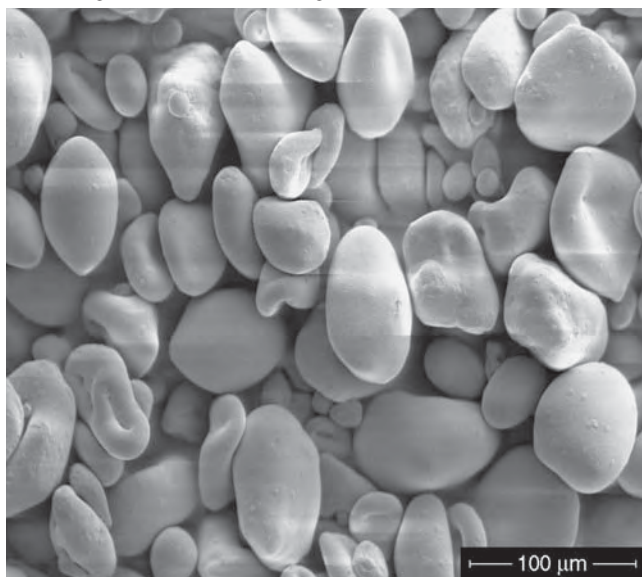
See Table I. See also Section 18.

10 Typical Properties

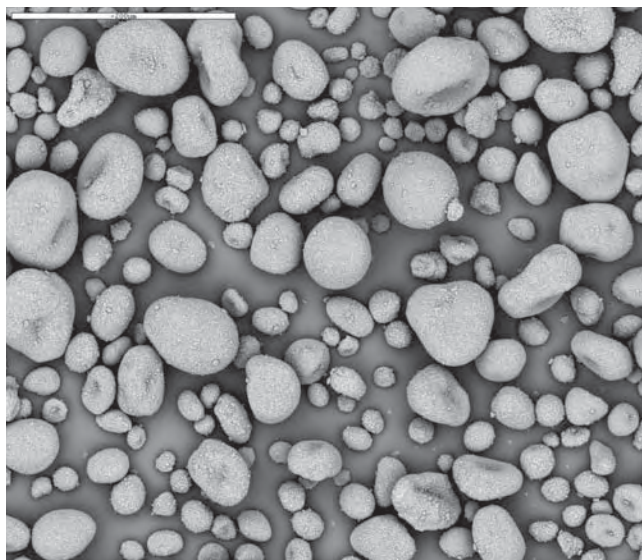
Acidity/alkalinity See Section 9.

Density (bulk)

SEM 1: Excipient: sodium starch glycolate (*Explotab*); manufacturer: JRS Pharma; magnification: 300 \times ; voltage: 5 kV.



SEM 2: Excipient: sodium starch glycolate (*Glycolys*); manufacturer: Roquettes Frères.



0.756 g/cm^3 for *Glycolys*;

0.81 g/cm^3 for *Primojel*;

0.67 g/cm^3 for *Tablo*.

Density (tapped)

0.945 g/cm^3 for *Glycolys*;

0.98 g/cm^3 for *Primojel*;

0.83 g/cm^3 for *Tablo*.

Density (true)

1.56 g/cm^3 for *Primojel*;

1.49 g/cm^3 for *Tablo*.

Melting point Does not melt, but chars at approximately 200°C.

NIR spectra see Figure 1.

Particle size distribution 100% of particles less than 106 μm in size. Average particle size (d_{50}) is 38 μm and 42 μm for *Primojel* by microscopy and sieving, respectively.

Solubility Practically insoluble in methylene chloride. It gives a translucent suspension in water.

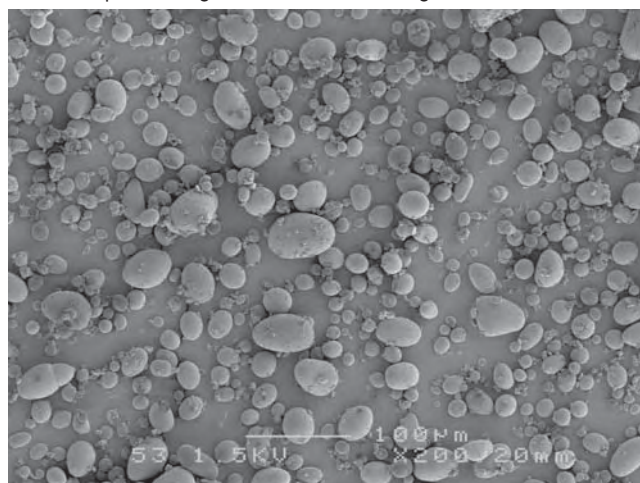
Specific surface area

0.24 m^2/g for *Glycolys*;

0.185 m^2/g for *Primojel*;

0.335 m^2/g for *Tablo*.

SEM 3: Excipient: sodium starch glycolate (*Primojel*); manufacturer: DMV-Fonterra Excipients; magnification: 200 \times ; voltage: 1.5 kV.



SEM 4: Excipient: sodium starch glycolate (*Vivastar P*); manufacturer: JRS Pharma; magnification: 300 \times ; voltage: 5 kV.

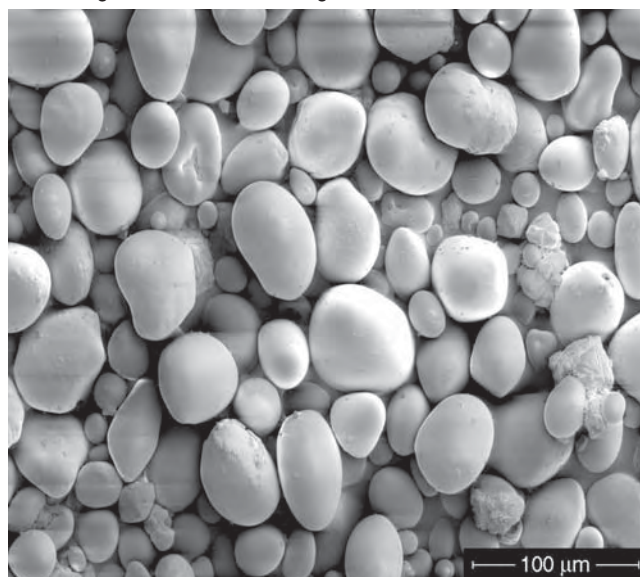


Table I: Pharmacopeial specifications for sodium starch glycolate.

Test	PhEur 6.0	USP32-NF27
Identification	+	+
Characters	+	—
Appearance of solution	+	—
pH	+	+
Type A	5.5–7.5	5.5–7.5
Type B	3.0–5.0	3.0–5.0
Type C	5.5–7.5	—
Heavy metals	≤20 ppm	≤0.002%
Iron	≤20 ppm	≤0.002%
Loss on drying	+	≤10%
Type A	≤10.0%	—
Type B	≤10.0%	—
Type C	≤7.0%	—
Microbial limits	+(a)	+(a)
Sodium chloride	+	≤7.0%
Type A	≤7.0%	—
Type B	≤7.0%	—
Type C	≤1.0%	—
Sodium glycolate	+	≤2.0%
Type A	≤2.0%	—
Type B	≤2.0%	—
Type C	≤2.0%	—
Assay (of Na)	+	+
Type A	2.8–4.2%	2.8–4.2%
Type B	2.0–3.4%	2.0–3.4%
Type C	2.8–5.0%	—

(a) Complies with tests for *Salmonella* and *Escherichia coli*.

Swelling capacity In water, sodium starch glycolate swells to up to 300 times its volume.

Viscosity (dynamic) ≤200 mPa s (200 cP) for a 4% w/v aqueous dispersion; viscosity is 4.26 mPa s for a 2% w/v aqueous dispersion (depending on source and grade).

11 Stability and Storage Conditions

Tablets prepared with sodium starch glycolate have good storage properties.^(22–24) Sodium starch glycolate is stable although very hygroscopic, and should be stored in a well-closed container in order to protect it from wide variations of humidity and temperature, which may cause caking.

The physical properties of sodium starch glycolate remain unchanged for up to 3 years if it is stored at moderate temperatures and humidity.

12 Incompatibilities

Sodium starch glycolate is incompatible with ascorbic acid.⁽²⁵⁾

13 Method of Manufacture

Sodium starch glycolate is a substituted derivative of potato starch. Typically, commercial products are also crosslinked using either sodium trimetaphosphate (Types A and B) or dehydration (Type C).⁽²⁶⁾

Starch is carboxymethylated by reacting it with sodium chloroacetate in an alkaline, nonaqueous medium, typically denatured ethanol or methanol, followed by neutralization with citric acid, acetic acid, or some other acid. *Vivastar P* is manufactured in methanolic medium, and *Explotab* in ethanolic medium.

14 Safety

Sodium starch glycolate is widely used in oral pharmaceutical formulations and is generally regarded as a nontoxic and nonirritant material. However, oral ingestion of large quantities may be harmful.

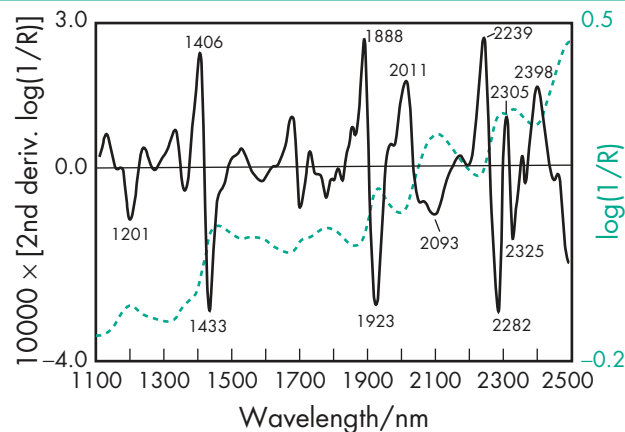


Figure 1: Near-infrared spectrum of sodium starch glycolate measured by reflectance.

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Sodium starch glycolate may be irritant to the eyes; eye protection and gloves are recommended. A dust mask or respirator is recommended for processes that generate a large quantity of dust.

16 Regulatory Acceptance

Included in the FDA Inactive Ingredients Database (oral capsules and tablets). Included in nonparenteral medicines licensed in the UK. Included in the Canadian List of Acceptable Non-medicinal Ingredients.

17 Related Substances

Pregelatinized starch; starch.

18 Comments

Sodium starch glycolate is one of the materials that have been selected for harmonization by the Pharmacopeial Discussion Group. For further information see the General Information Chapter <1196> in the USP32–NF27, the General Chapter 5.8 in PhEur 6.0, along with the ‘State of Work’ document on the PhEur EDQM website, and also the General Information Chapter 8 in the JP XV.

The physical properties of sodium starch glycolate, and hence its effectiveness as a disintegrant, are affected by the degree of crosslinkage, extent of carboxymethylation, and purity.^(27,28)

Sodium starch glycolate has been reported to interact with glycopeptide antibiotics,^(29,30) basic drugs, and increase the photostability of norfloxacin.⁽³¹⁾ The solubility of the formulation matrix and mode of incorporation in wet granulation can affect the disintegration time; disintegration times can be slower in tablets containing high levels of soluble excipients.⁽³²⁾

Commercially, sodium starch glycolate is available in a number of speciality grades, e.g. low pH (*Explotab Low pH*, *Glycolys Low pH*); low viscosity (*Explotab CLV*, *Glycolys LV*); low solvent (*Vivastar PSF*); and low moisture *Glycolys LM*.

A specification for sodium starch glycolate is included in the *Japanese Pharmaceutical Excipients* (JPE).⁽³³⁾

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22 Date of Revision

3 February 2009.

Sodium Stearyl Fumarate

1 Nonproprietary Names

BP: Sodium Stearyl Fumarate
PhEur: Sodium Stearyl Fumarate
USP-NF: Sodium Stearyl Fumarate

2 Synonyms

Fumaric acid, octadecyl ester, sodium salt; natrii stearyl is fumaras; *Pruv*; sodium monostearyl fumarate.

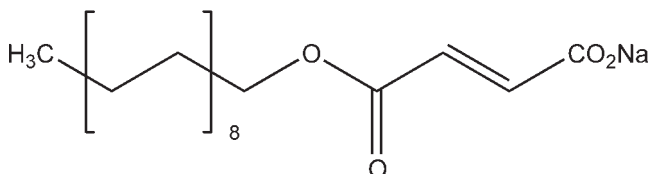
3 Chemical Name and CAS Registry Number

2-Butenedioic acid, monooctadecyl ester, sodium salt [4070-80-8]

4 Empirical Formula and Molecular Weight

$C_{22}H_{39}NaO_4$ 390.5

5 Structural Formula



6 Functional Category

Tablet and capsule lubricant.

7 Applications in Pharmaceutical Formulation or Technology

Sodium stearyl fumarate is used as a lubricant in capsule and tablet formulations at 0.5–2.0% w/w concentration.^(1–9) It is also used in certain food applications; *see* Section 16.

8 Description

Sodium stearyl fumarate is a fine, white powder with agglomerates of flat, circular-shaped particles.

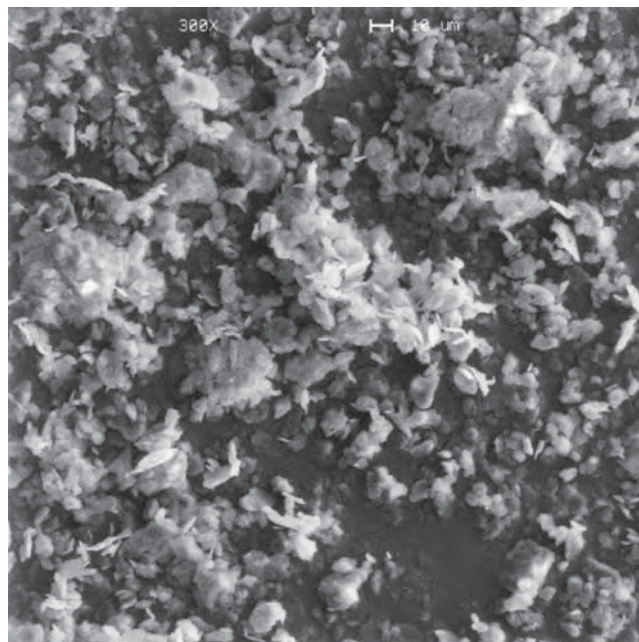
9 Pharmacopeial Specifications

See Table I.

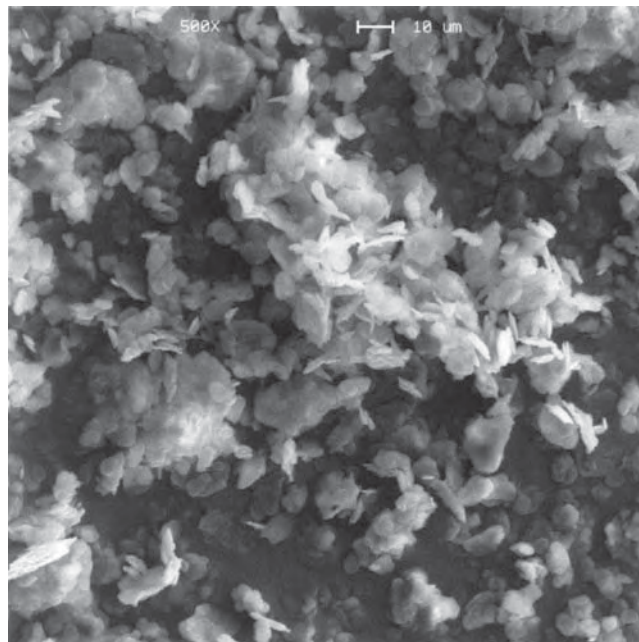
Table I: Pharmacopeial specifications for sodium stearyl fumarate.

Test	PhEur 6.0	USP32–NF27
Identification	+	+
Characters	+	—
Water	≤5.0%	≤5.0%
Lead	—	≤0.001%
Heavy metals	—	≤0.002%
Related substances	≤5.0%	—
Sodium stearyl maleate	—	≤0.25%
Stearyl alcohol	—	≤0.5%
Saponification value (anhydrous basis)	—	142.2–146.0
Assay (anhydrous basis)	99.0–101.5%	99.0–101.5%

SEM 1: Excipient: sodium stearyl fumarate; manufacturer: JRS Pharma LP; lot no.: 255-01; magnification: 300×.



SEM 2: Excipient: sodium stearyl fumarate; manufacturer: JRS Pharma LP; lot no.: 255-01; magnification: 500×.



10 Typical Properties

Acidity/alkalinity pH = 8.3 for a 5% w/v aqueous solution at 90°C.

Density 1.107 g/cm³

Density (bulk) 0.2–0.35 g/cm³

Density (tapped) 0.3–0.5 g/cm³