Titanium Dioxide

1 Nonproprietary Names

BP: Titanium dioxide
JP: Titanium oxide
PhEur: Titanii dioxidum
USP: Titanium dioxide

2 Synonyms

Anatase titanium dioxide; brookite titanium dioxide; color index number 77891; E171; *Kronos 1171*; pigment white 6; rutile titanium dioxide; *Tioxide*; *TiPure*; titanic anhydride; *Tronox*.

3 Chemical Name and CAS Registry Number

Titanium oxide [13463-67-7]

4 Empirical Formula and Molecular Weight

Empirical Formula	Molecular Weight
TiO_2	79.88

5 Structural Formula

TiO_2

6 Functional Category

Coating agent; opacifier; pigment.

7 Applications in Pharmaceutical Formulation or Technology

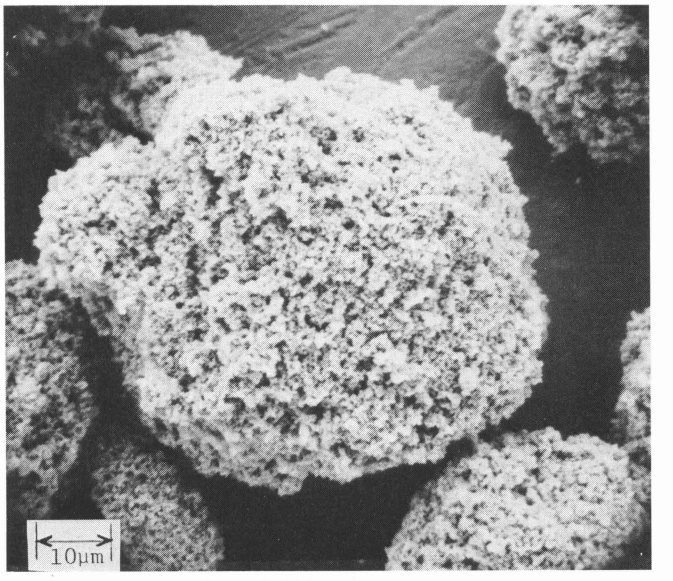
Titanium dioxide is widely used in confectionery, cosmetics, and foods, in the plastics industry, and in topical and oral pharmaceutical formulations as a white pigment.

Owing to its high refractive index, titanium dioxide has light-scattering properties that may be exploited in its use as a white pigment and opacifier. The range of light that is scattered can be altered by varying the particle size of the titanium dioxide powder. For example, titanium dioxide with an average particle size of 230 nm scatters visible light, while titanium dioxide with an average particle size of 60 nm scatters ultraviolet light and reflects visible light.[1]

In pharmaceutical formulations, titanium dioxide is used as a white pigment in film-coating suspensions,[2,3] sugar-coated tablets, and gelatin capsules. Titanium dioxide may also be admixed with other pigments.

Titanium dioxide is also used in dermatological preparations and cosmetics, such as sunscreens.[1,4]

SEM: 1
Excipient: Titanium dioxide
Magnification: 1200×
Voltage: 10 kV



8 Description

White, amorphous, odorless, and tasteless nonhygroscopic powder. Although the average particle size of titanium dioxide powder is less than 1 μm, commercial titanium dioxide generally occurs as aggregated particles of approximately 100 μm diameter.

Titanium dioxide may occur in several different crystalline forms: rutile; anatase; and brookite. Of these, rutile and anatase are the only forms of commercial importance. Rutile is the more thermodynamically stable and is used more frequently than the other crystalline forms.

9 Pharmacopeial Specifications

See Table I.

10 Typical Properties

Density (bulk): 0.4–0.62 g/cm^3 [5]
Density (tapped): 0.625–0.830 g/cm^3 [6]
Density (true):
3.8–4.1 g/cm^3 for Anatase
3.9–4.2 g/cm^3 for Rutile
Dielectric constant:
48 for Anatase
114 for Rutile
Hardness (Mohs):
5–6 for Anatase
6–7 for Rutile
See also Section 18.
Melting point: 1855°C

Table I: Pharmacopeial specifications for titanium dioxide.

Test	JP 2001	PhEur 2002	USP 25
Identification	+	+	+
Characters	—	+	—
Appearance of solution	—	+	—
Acidity or alkalinity	—	+	—
Water-soluble substances	≤5.0 mg	≤25 mg	≤0.25%
Antimony	—	+	—
Arsenic	≤10 ppm	≤5 ppm	≤1 ppm
Barium	—	+	—
Heavy metals	—	≤20 ppm	—
Iron	—	≤200 ppm	—
Loss on drying	≤0.5%	—	≤0.5%
Loss on ignition	—	—	≤13%
Acid-soluble substances	—	—	≤0.5%
Organic volatile impurities	—	—	+
Lead	≤60 ppm	—	—
Assay	≥98.5%	98.0–100.5%	99.0–100.5%

Moisture content: 0.44%

Particle size distribution: average particle size = 1.05 μm.[5] *See also* Figures 1 and 2.

Refractive index:
2.55 for Anatase
2.76 for Rutile

Specific heat:
0.71 J/g (0.17 cal/g) for Anatase
0.71 J/g (0.17 cal/g) for Rutile

Specific surface area: 9.90–10.77 m^2/g

Solubility: practically insoluble in dilute sulfuric acid, hydrochloric acid, nitric acid, organic solvents, and water. Soluble in hydrofluoric acid and hot concentrated sulfuric acid. Solubility depends on previous heat treatment; prolonged heating produces a less-soluble material.

Tinting strength (Reynolds):
1200–1300 for Anatase
1650–1900 for Rutile

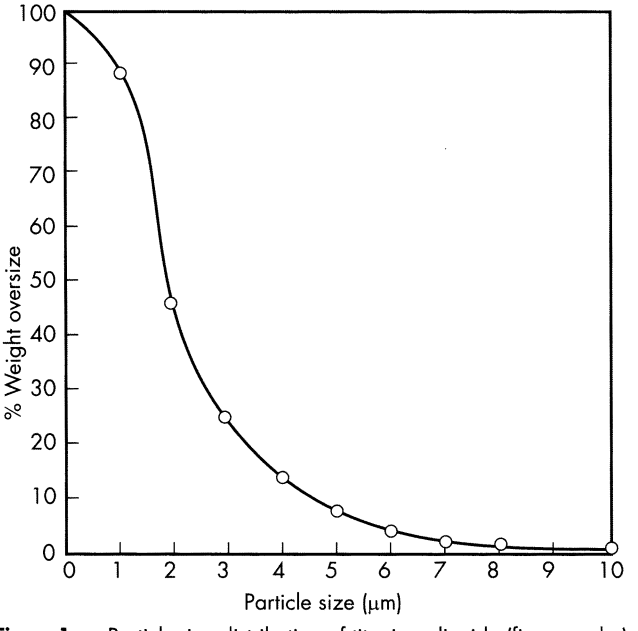


Figure 1: Particle-size distribution of titanium dioxide (fine powder).

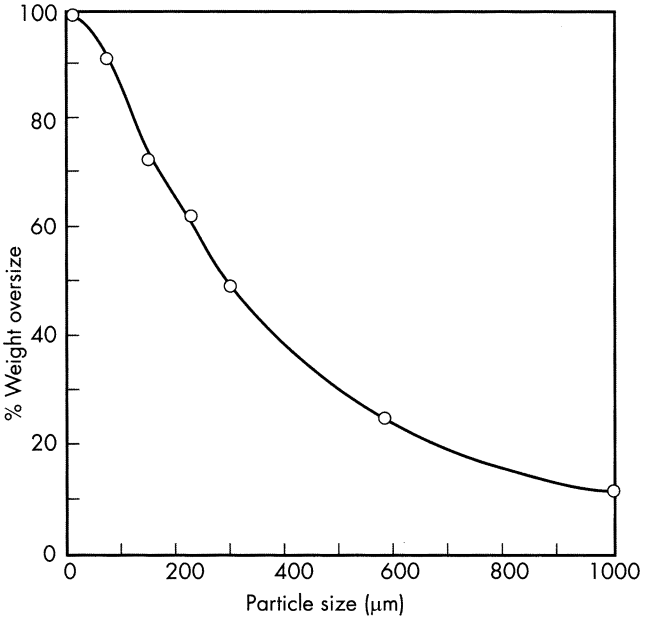


Figure 2: Particle-size distribution of titanium dioxide (agglomerated particles).

11 Stability and Storage Conditions

Titanium dioxide is extremely stable at high temperatures. This is due to the strong bond between the tetravalent titanium ion and the bivalent oxygen ions. However, titanium dioxide can lose small, unweighable amounts of oxygen by interaction with radiant energy. This oxygen can easily recombine again as a part of a reversible photochemical reaction, particularly if there is no oxidizable material available. These small oxygen losses are important because they can cause significant changes in the optical and electrical properties of the pigment.

Titanium dioxide should be stored in a well-closed container, protected from light, in a cool, dry place.

12 Incompatibilities

Owing to a catalytic effect, titanium dioxide may interact with certain active substances. Studies have shown that titanium dioxide monatonically degrades film mechanical properties and increases water vapor permeability of polyvinyl alcohol coatings when used as an inert filler and whitener.[6]

Titanium dioxide has also been shown to induce photooxidation of unsaturated lipids.[7]

13 Method of Manufacture

Titanium dioxide occurs naturally as the minerals rutile (tetragonal structure), anatase (tetragonal structure), and brookite (orthorhombic structure).

Titanium dioxide may be prepared commercially by direct combination of titanium and oxygen; by treatment of titanium salts in aqueous solution; by the reaction of volatile inorganic titanium compounds with oxygen; and by the oxidation or hydrolysis of organic compounds of titanium.

14 Safety

Titanium dioxide is widely used in foods and oral and topical pharmaceutical formulations. It is generally regarded as an essentially nonirritant and nontoxic excipient.

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Eye protection, gloves, and a dust mask are recommended. Titanium dioxide is regarded as a relatively innocuous nuisance dust,[8] that may be irritant to the respiratory tract. In the UK, the long-term (8-hour TWA) exposure limit is 10 mg/m^3 for total inhalable dust and 4 mg/m^3 for respirable dust.[9]

Titanium dioxide particles in the 500 nm range have been reported to translocate to all major body organs after oral administration in the rat.[10]

16 Regulatory Status

Accepted as a food additive in Europe. Included in the FDA Inactive Ingredients Guide (oral capsules, suspensions, tablets, and topical preparations). Included in nonparenteral medicines licensed in the UK.

17 Related Substances

Coloring agents.

18 Comments

Titanium dioxide is a hard, abrasive material. Coating suspensions containing titanium dioxide have been reported to cause abrasion and wear of a steel-coated pan surface, which led to white tablets being contaminated with black specks.[11]

If titanium dioxide is used as a pigment it should conform to the appropriate food standards specifications, which are more demanding than the pharmacopeial specifications.

When mixed with methylcellulose, titanium dioxide can reduce the elongation and tensile strength of the film but slightly increase the adhesion between pigmented film and the tablet surface.[12]

The EINECS number for titanium dioxide is 236-675-5.

19 Specific References

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20 General References

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21 Author

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22 Date of Revision

30 August 2002.