Carbon Dioxide

1 Nonproprietary Names

BP: Carbon dioxide
JP: Carbon dioxide
PhEur: Carbonei dioxidum
USP: Carbon dioxide

2 Synonyms

Carbonic acid gas; carbonic anhydride; E290.

3 Chemical Name and CAS Registry Number

Carbon dioxide [124-38-9]

4 Empirical Formula / Molecular Weight

CO_2 44.01

5 Structural Formula

CO_2

6 Functional Category

Aerosol propellant; air displacement.

7 Applications in Pharmaceutical Formulation or Technology

Carbon dioxide and other compressed gases such as nitrogen and nitrous oxide are used as propellants for topical pharmaceutical aerosols. They are also used in other aerosol products that work satisfactorily with the coarse aerosol spray that is produced with compressed gases, e.g., cosmetics, furniture polish, and window cleaners.[1–3]

The advantages of compressed gases as aerosol propellants are that they are inexpensive; are of low toxicity; and are practically odorless and tasteless. Also, in comparison to liquefied gases, their pressures change relatively little with temperature. However, the disadvantages of compressed gases are that there is no reservoir of propellant in the aerosol and pressure consequently decreases as the product is used. This results in a change in spray characteristics. Additionally, if a product that contains a compressed gas as a propellant is actuated in an inverted position, the vapor phase, rather than the liquid phase, is discharged. Most of the propellant is contained in the vapor phase and therefore some of the propellant will be lost and the spray characteristics will be altered. Also, sprays produced using compressed gases are very wet.

Carbon dioxide is also used to displace air from pharmaceutical products by sparging and hence to inhibit oxidation. As a food additive it is used to carbonate beverages and to preserve foods such as bread from spoilage by mold formation, the gas being injected into the space between the product and its packaging.[4,5]

Solid carbon dioxide is also widely used to refrigerate products temporarily, while liquid carbon dioxide, which can be handled at temperatures up to 31°C under high pressure, is used as a solvent for flavors and fragrances primarily in the perfumery and food manufacturing industries.

8 Description

Carbon dioxide occurs naturally as approximately 0.03% v/v of the atmosphere. It is a colorless, odorless, noncombustible gas with a faint acid taste. Solid carbon dioxide, also known as dry ice, is usually encountered as white-colored pellets or blocks.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for carbon dioxide.

Test	JP 2001	PhEur 2002	USP 25
Characters	+	+	—
Production	—	+	—
Carbon monoxide	—	+	—
Nitrogen monoxide and nitrogen dioxide	—	≤2ppm	—
Total sulfur	—	≤1 ppm	—
Water	—	≤67 ppm	≤5 ppm
Identification	+	+	+
Carbon monoxide	+	≤5 ppm	≤0.001%
Hydrogen sulfide	—	≤1 ppm	≤1 ppm
Sulfur dioxide	—	≤2 ppm	≤2.5 ppm
Nitrogen monoxide and nitrogen dioxide	—	≤2 ppm	≤2.5 ppm
Impurities	—	+	—
Limit of ammonia	—	—	≤0.0025%
Limit of nitric oxide	—	—	—
Acid	+	—	—
Hydrogen phosphide, hydrogen sulfide or reducing organic substances	+	—	—
Oxygen and nitrogen	+	—	—
Assay	≤99.50%	≤99.50%	≤99.00%

10 Typical Properties

Boiling point: −56.6°C
Critical pressure: 7.39 MPa (72.9 atm)
Critical temperature: 31.3°C
Density:
0.714 g/cm^3 for liquid at 25°C
0.742 g/cm^3 for vapor at 25°C
Flammability: nonflammable
Melting point: sublimes at −78.5°C
Solubility: 1 in about 1 of water by volume at normal temperature and pressure.
Vapor density (absolute): 1.964 g/m^3
Vapor density (relative): 1.53 (air = 1)
Vapor pressure: 6.436 MPa at 25°C
Viscosity (kinematic): 0.14 mm^2/s (0.14 cSt) at −17.8°C

11 Stability and Storage Conditions

Extremely stable and chemically nonreactive. Store in a tightly sealed cylinder. Avoid exposure to excessive heat.

12 Incompatibilities

Carbon dioxide is generally compatible with most materials although it may react violently with various metal oxides or reducing metals such as aluminum, magnesium, titanium, and zirconium. Mixtures with sodium and potassium will explode if shocked.

13 Method of Manufacture

Carbon dioxide is obtained industrially in large quantities as a by-product in the manufacture of lime; by the incineration of coke or other carbonaceous material; and by the fermentation of glucose by yeast. In the laboratory it may be prepared by dropping acid on a carbonate.

14 Safety

In formulations, carbon dioxide is generally regarded as an essentially nontoxic material.

See also Section 15.

15 Handling Precautions

Handle in accordance with standard procedures for handling metal cylinders containing liquefied or compressed gases. Carbon dioxide is an asphyxiant and inhalation in large quantities is hazardous. It should therefore be handled in a well-ventilated environment equipped with suitable safety devices for monitoring vapor concentration.

It should be noted that carbon dioxide is classified as a greenhouse gas responsible for global warming. At the present time there are no restrictions on its use for aerosols and other applications.

In the UK, the occupational exposure limits for carbon dioxide are 9150 mg/m^3 (5000 ppm) long-term (8-hour TWA) and 27 400 mg/m^3 (15 000 ppm) short-term (15-minute).[6] In the USA, the permissible exposure limits are 9000 mg/m^3 (5000 ppm) long-term and the recommended exposure limits are 18 000 mg/m^3 (10 000 ppm) short-term and 54 000 mg/m^3 (30 000 ppm) maximum, short-term.[7]

Solid carbon dioxide can produce severe burns in contact with the skin and appropriate precautions, depending on the circumstances and quantity of material handled, should be taken. A face shield and protective clothing, including thick gloves, are recommended.

16 Regulatory Status

GRAS listed. Accepted for use in Europe as a food additive. Included in the FDA Inactive Ingredients Guide (injections).

17 Related Substances

Nitrogen; nitrous oxide.

18 Comments

Supercritical carbon dioxide has been used in the formation of fine powders of stable protein formulations.[8,9]

Carbon dioxide has also been investigated for its suitability in Aerosol Solvent Extraction Systems (ASES), to generate microparticles of proteins suitable for aerosol delivery from aqueous based solutions.[10]

The EINECS number for carbon dioxide is 204-696-9.

19 Specific References

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