Nitrogen

1 Nonproprietary Names

BP: Nitrogen
JP: Nitrogen
PhEur: Nitrogenium
USPNF: Nitrogen

2 Synonyms

Azote; E941.

3 Chemical Name and CAS Registry Number

Nitrogen [7727-37-9]

4 Empirical Formula and Molecular Weight

N_2 28.01

5 Structural Formula

N_2

6 Functional Category

Aerosol propellant; air displacement.

7 Applications in Pharmaceutical Formulation or Technology

Nitrogen and other compressed gases such as carbon dioxide 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 produced with compressed gases, e.g., furniture polish and window cleaner. Nitrogen is insoluble in water and other solvents, and therefore remains separated from the actual pharmaceutical formulation.

Advantages of compressed gases as aerosol propellants are that they are inexpensive; of low toxicity; and practically odorless and tasteless. In contrast to liquefied gases, their pressures change relatively little with temperature. However, there is no reservoir of propellant in the aerosol and as a result the pressure decreases as the product is used, changing the spray characteristics.

Misuse of a product by the consumer, such as using a product inverted, results in the discharge of the vapor phase instead of the liquid phase. 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. Additionally, the sprays produced using compressed gases are very wet. However, recent developments in valve technology have reduced the risk of misuse by making available valves which will spray only the product (not propellant) regardless of the position of the container. Additionally, barrier systems will also prevent loss of propellant.

Nitrogen is also used to displace air from solutions subject to oxidation, by sparging, and to replace air in the headspace above products in their final packaging, e.g., in parenteral products packaged in glass ampoules. Nitrogen is also used for the same purpose in many food products.

8 Description

Nitrogen occurs naturally as approximately 78% v/v of the atmosphere. It is a nonreactive, noncombustible, colorless, tasteless, and odorless gas. It is usually handled as a compressed gas, stored in metal cylinders.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for nitrogen.

Test	JP 2001	PhEur 2002 (Suppl 4.2)	USPNF 20
Identification	+	+	+
Characters	—	+	—
Odor	—	—	+
Carbon monoxide	—	⩽5 ppm	⩽0.001%
Carbon dioxide	+	⩽300 ppm	—
Water	—	⩽67 ppm	—
Oxygen	—	⩽50 ppm	⩽1.0%
Assay	⩾99.5%	⩾99.5%	⩾99.0%

10 Typical Properties

Boiling point: −195.8°C
Critical pressure: 3.39 mPa (33.49 atm)
Critical temperature: −147.2°C
Density: 0.967 g/cm^3 for vapor at 21°C.
Flammability: nonflammable
Melting point: −210°C
Solubility: practically insoluble in water and most solvents; soluble in water under pressure.
Vapor density (absolute): 1.25 g/cm^3 at standard temperature and pressure.
Vapor density (relative): 0.97 (air = 1)

11 Stability and Storage Conditions

Nitrogen is stable and chemically unreactive. It should be stored in tightly sealed metal cylinders in a cool, dry place.

12 Incompatibilities

Generally compatible with most materials encountered in pharmaceutical formulations and food products.

13 Method of Manufacture

Nitrogen is obtained commercially, in large quantities, by the fractional distillation of liquefied air.

14 Safety

Nitrogen is generally regarded as a nontoxic and nonirritant material. However, it is an asphyxiant and inhalation of large quantities is therefore hazardous. *See also* Section 18.

15 Handling Precautions

Handle in accordance with procedures for handling metal cylinders containing liquefied or compressed gases. Eye protection, gloves, and protective clothing are recommended. Nitrogen is an asphyxiant and should be handled in a well-ventilated environment. The oxygen content of air in the working environment should be monitored and should not be permitted to fall below 19% v/v at normal atmospheric pressure.[1]

16 Regulatory Status

GRAS listed. Accepted for use as a food additive in Europe. Included in parenteral and nonparenteral medicines licensed in the UK and USA.

17 Related Substances

Carbon dioxide; nitrous oxide.

18 Comments

Different grades of nitrogen are commercially available that have, for example, especially low moisture levels.

Nitrogen is commonly used as a component of the gas mixtures breathed by divers. Under high pressure, such as when diving at great depths, nitrogen will dissolve in blood and lipid. If decompression is too rapid, decompression sickness may occur when the nitrogen effervesces from body stores to form gas emboli.

The EINECS number for nitrogen is 231-783-9.

19 Specific References

1 Health and Safety Executive. *EH40/2002: Occupational Exposure Limits 2002*. Sudbury: Health and Safety Executive, 2002.

20 General References

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22 Date of Revision

10 October 2002.