MINISTRY OF HEALTH OF THE RUSSIAN FEDERATION

GENERAL PHARMACOPOEIA MONOGRAPH

Gas chromatography

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Gas chromatography is a method for the separation of volatile compounds, based on the difference in the distribution of analyzed mixture components in the system of immiscible phases moving relative to each other, where a gas (carrier gas) acts as a mobile phase and a solid or liquid sorbent applied to the solid carrier or the inner walls of the column is used as a stationary phase.

Scope

In pharmaceutical analysis, gas chromatography is used to assess purity, for identification and assay of drug products in tests "Related substances", "Uniformity of Dosage", "Dissolution", "Assay", "Residual organic solvents" etc.

Equipment

A gas chromatograph apparatus includes a sample injection unit (injector), a thermostat with a chromatographic column, a detector and a data acquisition and data processing system. A carrier gas from a pressurized container passes through a sample injector, a column and then through a detector.

Chromatography is carried out at a constant temperature, or in accordance to a predetermined temperature program.

Sample injector

A liquid sample injection is performed by means of a syringe both directly into the column and into the vaporization chamber that can be equipped with a sample splitter.

A gas phase injection is performed using the equipment for a static or dynamic headspace analysis. The headspace analysis can improve the sensitivity of detection of volatile compounds.

In a *static headspace analysis*, a hermetically closed vessel containing a solid or liquid sample is placed in a thermostatic chamber and heated for a certain period of time to achieve the equilibrium between the two phases. After the equilibrium is achieved, a certain amount of the gas phase is withdrawn from the vessel and is introduced into the chromatograph evaporator.

In a dynamic headspace analysis (stripping), an inert gas is purged through the sample during a certain time. Volatile components are purged from the sample and are concentrated on the sorbent in a trap. After this, the trap quickly heats up, and volatile components are transferred with a stream of inert gas into the chromatographic column.

Columns

There are several types of analytical columns: packed, micropacked, capillary, multicapillary.

Packed columns are made of metal (stainless steel), glass, polytetrafluoroethylene, shaped into a spiral. The inner diameter of packed columns is from 2 to 4 mm, and the length is from 0.5 to 5.4 m.

The carrier gas flow rate may be set within the range of 10 to 60 ml/min.

Micropacked columns differ from packed columns only by a tube diameter equal to 0.5-1.0 mm. The length of the columns is typically 0.5 to 2 m.

Capillary columns are made of fused silica or metal. An inner diameter is from 0.10 mm to 0.53 mm, the length is from 5 to 200 m, the thickness of the stationary liquid phase is from 0.1 to 5.0 microns.

The carrier gas flow rate may be set within the range of 1 to 5 ml/min.

Multicapillary columns represent sets of parallel capillaries with an inner diameter of about 40 microns, length of 1 m, and a total number of 1000 or more.

Stationary phases

Gas chromatography can be subdivided into two types: gas adsorption and gas-liquid chromatography. Gas-liquid chromatography is the most widely used in pharmaceutical analysis.

In *gas-solid chromatography,* inorganic (silica gel — Spherosil, Porasil, Silihrom, etc.; graphitized carbon blacks — Carbopak C and B, Carbosil, Carbospher; molecular sieves — sodium and calcium aluminosilicates) and porous polymeric sorbents are used as sorbents (adsorbents).

In gas-liquid chromatography, a stationary phase (absorbent) is a liquid applied onto a solid carrier. A carrier is a relatively inert adsorbent with a low specific surface on which the stationary phase should be retained as a film with uniform thickness. Mineral and polymeric carriers are used. Most mineral carriers are processed diatomites. Carriers with a particle size ranging from 125 microns to 150 or 150 to 180 microns are commonly used.

In capillary columns, a sorbent is applied to the inner capillary surface as a layer of liquid or stationary phase or as an adsorbent layer, the role of which is often carried by a polymeric film.

Mobile phase

Nitrogen, helium, argon or hydrogen is used as the mobile phase. These carrier gases can be fed into a system consisting either of cylinders or of gas generators, allowing to obtain a high purity gas.

Detectors

A large number of detectors is available for gas chromatography: flame ionization detector (FID), thermal conductivity detector (TCD), thermionic (TTI), electron capture detector (ECD), mass spectrometric detector etc.

The choice of a detector is determined by its basic characteristics (sensitivity, detection limit, linearity, speed and selectivity), which are most relevant to the purpose of the analysis and its conditions.

By virtue of versatility, superior characteristics and high performance, a flame ionization detector and a thermal conductivity detector became the most widely used in the analysis of drug products.

Method

A gas chromatography analysis is carried out in accordance with the set parameters of the chromatographic system. The combination of these parameters is called a method.

The method description should specify the following: detector type, column type (packed or capillary), material and geometrical parameters of the column, sorbent (solid carrier type and its characteristics, stationary liquid phase and its amount), sample injection method and its parameters, temperature of the evaporator, column and detector, gas-carrier and its flow rate.

The evaluation of chromatographic separation is carried out based on the system suitability test provided in pharmacopeial monograph.

In order to achieve compliance with system suitability requirements, some parameters may be within the specified limits provided in GM Chromatography.