LYOPHILIZATION AS A METHOD OF LIPOSOMAL DRUGS STABILIZATION

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In the pharmaceutical market, liposomal preparations are represented by lyophilized forms, due to the fact that lyophilization allows to stabilize nanoscale, to provide a longer shelf life of liposomes, to avoid increasing the oxidation index of lipid components.

Lyophilization is based on the sublimation process – the transition of moisture from the solid state (ice) to gaseous (water vapour), omitting the liquid phase. Sublimation drying has a number of significant advantages over other approaches: the ability to dry finished dosage forms in ampoules or vials under aseptic conditions; hermetization can be carried out in a protective gas atmosphere; the moisture content in the product can reach extremely low levels; high stability and viability of the lyophilized material. Disadvantages include the inability to lyophilize the product, which requires supercooling to form ice, or when frozen, a film is formed on the surface, which prevents the release of moisture vapor.

The lyophilization process is carried out in four stages: 1) pre-freezing; 2) primary drying (sublimation in vacuum); 3) secondary drying (additional drying); 4) completion of the drying process. Characteristics of unsatisfactory lyophilic drying of biological products are: the appearance of bubbles on the material surface as a result of the presence of some liquid in the frozen mass; irregular porosity; significant reduction in volume compared to the initial volume; unsatisfactory separation of dry mass from the walls of ampoules and vials; unsatisfactory solubility of dried material.

The process of liposomal drugs lyophilization is determined by a number of factors: the size and charge of liposomes, phospholipid composition and physicochemical properties of the substance introduced into liposomes, the structure of the bilayer and other factors. As a result, the lyophilization process conditions must be determined for each proposed drug.

In order to determine the optimal process conditions of lyophilization of the liposomal form of bioflavonoids, the eutectic temperature, the freezing temperature, cryoprotectant concentration, and secondary drying temperature were determined. Freezing and freeze-drying of the liposomal composition of bioflavonoids was carried out in a sublimation equipment Epsilon 2-6-D LSCPlus.

Pre-freezing was performed to a temperature of minus 35±2 °C. Lactose at a concentration of 4 % was chosen as a cryoprotectant. Sublimation of water was initiated by gradually reducing of the pressure to 0.1 mBar. To remove the absorbed water from the product, secondary drying was performed at 30±2 °C.

The time of emulsion formation, nanoparticle size, level of bioflavonoids encapsulation, water content in lyophilisate were monitored. The selected lyophilization program ensured the preservation of nanoscale liposomes and a moisture content of 2.1–2.3 %.