DEVELOPMENT OF STATE PHARMACOPOEIA OF UKRAINE MONOGRAPH "DIACAMPH"

Podgayniy D.G., Merzlikin S.I.
National University of Pharmacy, Kharkiv, Ukraine
podgayniy@list.ru

Antidiabetic agent Diacamph tablets 0.250 g, designed in NPhU, according to the decisions made by the scientific advisory council of State Pharmacological Center of Ministry of Healthcare of Ukraine from 26.02.2004 r. allowed for medical use.

For the introduction into manufacture it was appropriate to develop of SPU monograph "Diacamph" for the active pharmaceutical ingredient. In order to fulfill this task five series of diacamph were synthesized by the way of receipt, regularized of relevant technological documentation. Diacamph by formula – $C_{16}H_{20}N_2O_2$, by molecular weight – 272.35, by chemical name – (±)-cys-3-(2'-benzimidazolyl)-1,2,2-trimethylcyclopenthancarboxilic acid, contains basic substance – from 98.5 % to 101.0 %, which is a crystalline powder, white or nearly white, practically insoluble in water R, soluble in 96 % alcohol R, little soluble in methylene chloride R, $T_{m.p.}$ about 255 °C. Identification. 1. UV absorption spectrum of 0.001% diacamph solution in 96% alcohol R in the range from 220 nm to 300 nm has three absorption maxima at wavelengths of 247 nm±2, 276±2 nm and 283±2 nm. 2. IR spectrum of diacamph in disks with KBr (1 mg of substance in 300 mg KBr) has the characteristic bands of valence and deformation vibrations at 750, 1470, 3430, 2980, 1295, 1690 cm^{-1}. 3. TLC: stationary phase – plate Merck (silica gel GF_{254}), mobile phase – ether R – formic acid anhydrous R – 96% alcohol R – water R (90:7:10:3), developer – potassium iodobismuthate R2 solution (solution for spraying). In the chromatogram of test solution the main spot is manifested at WSS of diacamph spots (Rf ~ 0,31), corresponding in size and color. 4. Reaction of formation of ammonium salt with copper (II) sulfate R (reaction for carboxyl group, blue precipitate). Impurities (TLC in the above conditions). In the chromatogram of test solution (100 μg of diacamph), any spot other than the principal (Rf~0,31) is not intense than spot on the chromatogram of reference solution (100 μg of diacamph WSS) by size and color. The content of heavy metals in the synthesized samples did not exceed 0.001% (10 ppm). Loss in weight on drying not more than 1.0%. The content of sulfated ash – less than 0.1%. Assay. Potentiometric titration in glacial acetic acid medium by 0.1 M solution of perchloric acid R and titration by 0.1 M sodium hydroxide solution R. The powder of diacamph stored in a dark place. The technological impurities of diacamph: α-2'-aminophenylamid of (±)-cys-1,2,2-trimethylcyclopenthancarboxilic acid and lactam of (±)-cys-3-(2'-benzimidazolyl)-1,2,2-trimethylcyclopenthancarboxilic acid.