Abstract

Nowadays, the pharmaceutical regulatory entities are paying special attention to the topic of the residual solvents in the active ingredients (AI). D-004 is a new AI obtained from the Cuban royal palm (Roystonea regia) fruits, which has been shown to be effective in experimental models of prostate hyperplasia. Taking into account the use of n-hexane for obtaining this AI, a new limit test method, based on Static Headspace/GC-MS (SHS/GC-MS), was developed and validated for determining this residual solvent. Six batches of D004 were used. For preparing samples, 1 mL of D-004 was placed into 10 mL vial and heated at 80 °C for 1 hour. Afterwards, 1 mL of the head space was immediately injected into the GC-MS. The n-hexane concentrations were determined by interpolating the n-hexane average responses in the calibration curve of the linearity test and limit concentration was established at 60 ppm. The proposed method for determining n-hexane as residual solvent in D004 AI was found suitable sensitive, specific, linear (correlation coefficient > 0.999 and R.S.D. of slope < 2.4 %) and precise (RSD < 8 %). Concentrations between 1.6 and 52 ppm were determined with a detection limit of 0.26 ppm. The validated limit test method allowed determining residual n-hexane concentrations, which were < 60 ppm, values that were lower than that established by the ICH (290 ppm). The method was found suitable for quality control of residual n-hexane in D004 AI.

Keywords

D-004, residual solvent, headspace, GC-MS, limit test.