METHOD DEVELOPMENT AND VALIDATION FOR ESTIMATION OF RESIDUAL SOLVENTS IN IVABRADINE BY GC-HS-FID

 **P. Rajani1, Narmada Vallakeerthi1\*, A. Ravinder Nath1, P. Muralidhar Reddy2\***

¹Department of Pharmacy, Pharmaceutical Analysis and Quality Assurance, University College of Technology(A), Osmania University, Hyderabad, Telangana – 500007, India

2Department of Chemistry, University College of Science, Osmania University, Hyderabad, Telangana– 500007, India.

**1First Author:** **rajanisatya316@gmail.com**

**\*1, 2 Corresponding authors:** **rishikravi@gmail.com****, pmdreddy@gmail.com**

**Abstract**. Solvent selection is very crucial step in the drug development and manufacturing in the pharmaceutical industry because these may affect the physicochemical properties and these may be hazardous to human health. Residual solvents should be within the limits given by the ICH and measuring residual solvents is crucial for the release testing of all the active pharmaceutical ingredients to follow the good manufacturing practices (GMP).

Ivabradine is a hyperpolarization-activated cyclic nucleotide- gated channel blocker used to treat heart failure. The residual organic solvents (dichloromethane, tetrahydrofuran, toluene, Xylene) in ivabradine API was analyzed.

Residual solvents in ivabradine API are estimated by static head space chromatography (HS-GC) coupled with a flame ionization detector (FID) was developed and validated for the estimation of residual solvents dichloromethane, toluene, xylene, tetrahydrofuran in ivabradine API. Dimethyl sulfoxide is used as diluent and optimized chromatogram was established by using DB-624 column, (30mx0.53mm) 3.0µm column, injector and detector temperatures are 160°C and 250°C, with a hold time of 3.0 min. by maintaining the flow rate of 1.2 ml/min. with a split ratio of 5:1 and total run time is 15 min. and carrier gas used is nitrogen. This developed method is validated as per the ICH guidelines and the parameters are system suitability, specificity, linearity and range, accuracy, precision, limit of detection and quantitation, and robustness are within the acceptable limits as per the guidelines given by the ICH.

**Keywords:** Development, validation, Residual solvents, Ivabradine

References:

[1] ICH Q3A (R2) Impurities in new drug substances - Scientific guideline | European Medicines Agency.” https://www.ema.europa.eu/en/ich-q3a-r2-impurities-new-drug-substances-scientific-guideline (accessed Nov. 27, 2022).

[2] C. B’Hymer, “Residual solvent testing: a review of gas-chromatographic and alternative techniques,” *Pharm Res*, vol. 20, no. 3, pp. 337–344, Mar. 2003, Doi: 10.1023/A:1022693516409.

[3] “Q3C(R8) Impurities: Guidance for Residual Solvents Guidance for Industry | FDA.” https://www.fda.gov/regulatory-information/search-fda-guidance-documents/q3cr8-impurities-guidance-residual-solvents-guidance-industry (accessed Nov. 27, 2022).