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Research Article

DEVELOPMENT AND VALIDATION OF RESIDUAL SOLVENT ANALYSIS FOR ISOPROPYL ALCOHOL FROM TOLPERISONE HYDROCHLORIDE SUSTAINED RELEASE TABLET USING GAS CHROMATOGRAPHY

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ABSTRACT

In the current work, a Gas Chromatography method is developed and validated for residual analysis of solvent from Tolperisone Hydrochloride Sustained Release Tablets (450 mg). A Gas Chromatography system equipped with FID detector and Headspace sampler was used for the analysis. The method was developed using DB-624 column of length 30 m, ID 0.32 mm and film thickness of 1.8 µm equivalent to USP G43. The total run time for the method was 44.4 mins. The method was validated for parameters according to USP official method given in chapters of USP 467; Method IV. These methods include parameters like Specificity, Precision, System precision, method Precision, Ruggedness and System suitability.

INTRODUCTION

Tolperisone, a piperidine derivative, is a centrally acting muscle relaxant. In Tolperisone is indicated for use in the treatment of pathologically increased tone of the cross-striated muscle caused by neurological diseases (damage of the pyramidal tract, multiple sclerosis, myelopathy, encephalomyelitis) and of spastic paralysis and other encephalopathy manifested with muscular dystonia.

For pharmacopeial purposes, residual solvents in pharmaceuticals are defined as organic volatile chemicals that are used or produced in the manufacture of drug substances or excipients, or in the preparation of drug products. The residual solvents are not completely removed by practical manufacturing techniques. Appropriate selection of the solvent for the synthesis of a drug substance or an excipient may enhance the yield, or determine characteristics such as crystal form, purity, and solubility. Therefore, the solvent may sometimes be a critical element in the synthetic process.

MATERIALS AND METHODS

MATERIALS

Isopropyl alcohol and N,N-Dimethylformamide both of HPLC grade purchased from Merck (Darmstadt, Germany).

Sampling

150 tablets of Tolperisone Hydrochloride Sustained Release Tablets 450 mg were selected at random from Batch No. TOLT – 450 – 1008020.

Chemical and Standard Solution Preparations

Standard Solution

Standard solution of isopropyl alcohol was prepares by weighing 500 mg of HPLC grade Isopropyl alcohol into to a 100 mL standard flask. The volume was make up to 100 mL using N,N-Dimethylformamide. 20 mL of this solution was further diluted to 100 mL using N,N-Dimethylformamide in another standard flask. 5 mL of this solution was taken into headspace vial, crimped and placed in the headspace.

Blank Solution
A blank solution of N,N-Dimethylformamide was prepared by taking 5 mL of the HPLC grade N,N-Dimethylformamide solution directly in the headspace vial, crimped and placed in the headspace.

Sample Solution
From the selected sample tablets, 10 tablets were taken at random. They were ground to consistency of fine powder using a mortar pestle. From this powder 1000 mg portion was accurately weighed and transferred to headspace vial. To this vial, 5 mL of N,N-Dimethylformamide was added. The vial was crimped, sonicated for 20 minutes and then used for analysis.

Instrumentation and Chromatographic Conditions
A Gas chromatographic system equipped with FID detector and Headspace sampler. USP G43 equivalent column DB-624 capillary column of 30 m length, 0.32 mm internal diameter and 1.8 µm film thickness, manufactured by Agilent Technologies was used for chromatographic separation. The sample injections were done in splitless mode. The flow rate for Hydrogen gas was set to 40 mL/min, Air to 400 mL/min and Nitrogen to 35 cm/sec. Injector temperature was set to 140˚ C, detector temperate was set to 260˚ C. Oven programming was done as follows: Initial temperature of 40˚ C held for 20 minutes, increased to 240˚ C at ramp rise of 45˚ /min and maintained to 240˚ C for 20 minutes. The total run time for analysis was 44.4 minutes. Headspace sampler was programmed as, oven temperature at 85˚ C, needle temperature at 100˚ C, transfer line temperature at 105˚ C, equilibration time of 60.0 minutes, pressurization time of 2.0 minutes and injection volume 0.1 mL, 0.05 minutes.

Method Validation
System Suitability
System suitability tests were carried out to ensure reproducibility of the equipment. The tests were carried out by injecting standard solution in 6 replicates, single injection of blank solution and test solution.

Specificity
Specificity is the ability to assess unequivocally the analyte in the presence of other components which may be expected to be present. The tests were carried out by injecting standard solution in 6 replicates, single injection of blank solution and test solution.

Precision
Precision is the measure of either the degree of reproducibility or of repeatability of the analytical method under normal conditions. The test were carried out in one set at 100 % of the test concentration and spiked.
System precision was carried out with 6 readings of standard solution.
Method precision was carried out using one sample of 100 % concentration and 6 samples of spiked test solutions.

Recovery
The spiked sample was prepared using 20 tablets from the same batch no. These tablets were ground to fine powder using a mortar pestle. From this powder 1000 mg portion was accurately weighed and transferred to headspace vial. To this vial, 5 mL of N,N-Dimethylformamide was added. The vial was crimped and sonicated for 20 minutes.

Ruggedness
Ruggedness expresses within laboratories variation in terms of different days, different analyst, different equipment, etc. Different analyst performed the analysis using fresh standard and sample solution on different days and equipments.

RESULTS AND DISCUSSION
Isopropyl alcohol belongs to Class 3 residual solvents as per USP. The permitted daily exposure for this solvent is 50.0 mg/day while the concentration limit is 5000 ppm. The analyte peak was well separated and resolved from the sample. The retention time was found to be at 4.11 min. The average concentration of isopropyl alcohol in sample was found to be 4904.6 ppm.

System Suitability
The method was found to be suitable for the proposed analysis as the relative standard deviation of average peak area of system suitability test is not more than 15.0 %.

Specificity
Retention time obtained with test sample is comparable to the retention time obtained for the standard. All peaks are well separated from each other indicating the specificity of the analytical method for Tolperisone Hydrochloride Sustained Release Tablets 450 mg.

Precision
Precision measured at all level was within the acceptable criterion indicating the efficiency of method for the proposed analysis.

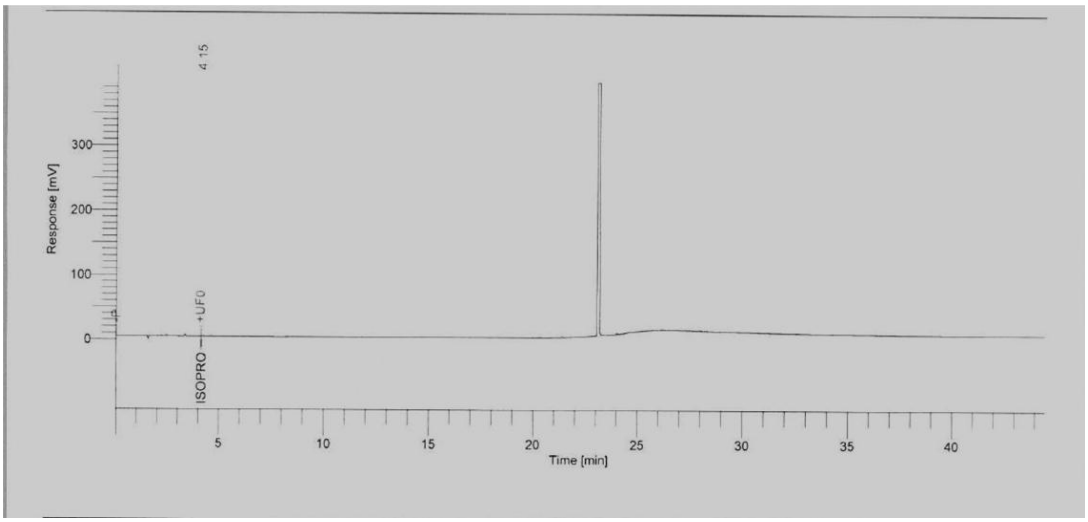

Fig. 1: Chromatogram of Diluent

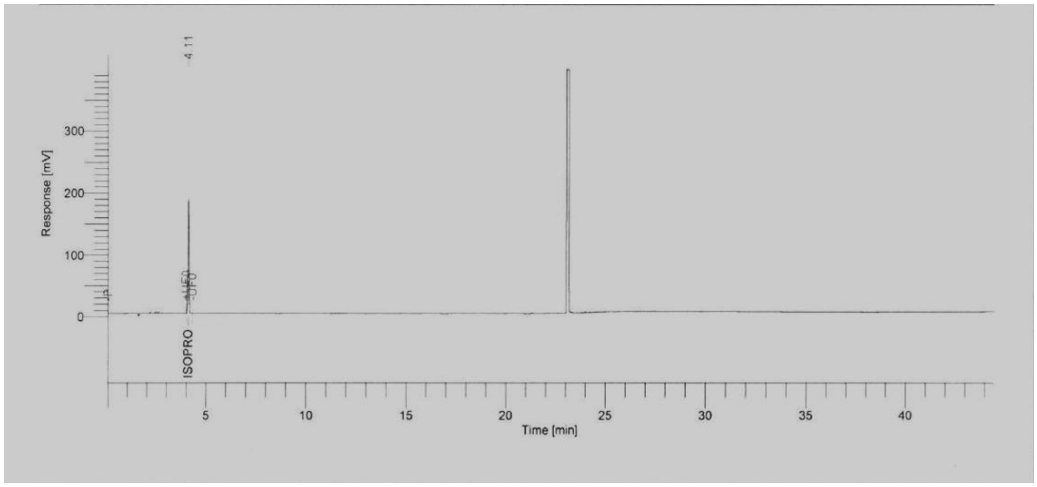

Fig. 2: Chromatogram of Analyte Solvent Standard

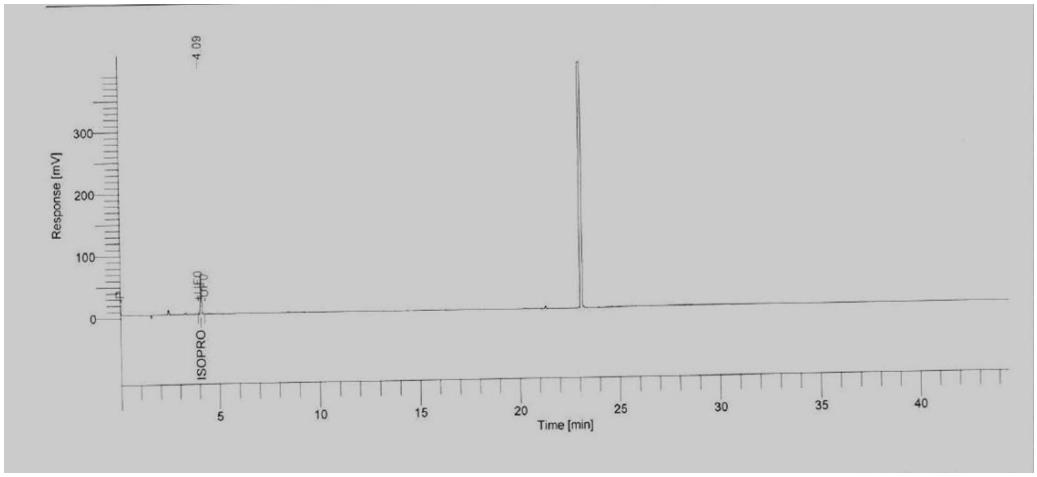

Fig. 3: Chromatogram of Analyte Solvent from Tablet

Recovery

The recovery for the samples was found between 90 – 110%. The mean % obtained for Isopropyl alcohol is 103.2. The % RSD was found to be 1.12 %.

Thus the method is precise for isopropyl alcohol.

CONCLUSION

Residual analysis is an integral part of pharmaceutical analysis. Residual solvents in pharmaceuticals, commonly known as organic volatile impurities (OVIs), are chemicals that are either used or produced during the manufacture of active pharmaceutical ingredients (APIs), excipients and drug products. OVIs may also contaminate products during packaging, storage in warehouses and/or during transportation. Because residual solvents have no therapeutic benefits but may be hazardous to human health and the environment, it must be ensured that they are either not present in products or are only present below recommended acceptable levels. The method was found to be simple, precise, accurate and specific and can be used for routine quality control for the quantification of this compound in the pharmaceutical product.

REFERENCES

USP Chapter 467 Residual Solvent Analysis.