STABILITY-INDICATING LC METHOD FOR MILNACIPRAN HYDROCHLORIDE CAPSULES

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Introduction: Milnacipran hydrochloride ($C_{15}H_{22}N_2O{\cdot}HCl$) is a selective serotonin and norepinephrine reuptake inhibitor (SNRI) indicated as antidepressant and for the management of fibromyalgia.
Objective: Considering that there are no official methods for the determination of the milnacipran hydrochloride capsules, it is necessary to develop and validate methods to ensure the quality of pharmaceutical formulation. The purpose of this study was to develop and validate a simple and fast stability-indicating LC method according to guidelines [1-3], which require the forced degradation of the active substance under several stress conditions.
Materials and Methods: A selective stability-indicating LC method was developed and validated using a Nucleosil C8 endcapped (150 mm × 4.6 mm, 100 Å, 5 µm) analytical column from Macherey-Nagel and a guard column Phenomenex (C18, 4 mm x 3 mm), a mobile phase consisting of acetonitrile, water and triethylamine (70 : 30 : 0.085, v/v/v), the pH value of the aqueous phase was adjusted to 7.5, a constant flow-rate of 1.2 $mL{\cdot}min^{-1}$ was used and the detector was operated at a wavelength of 210 nm. The interference from inactive ingredients was investigated by the analysis of a blank pharmaceutical formulation. Potential degradation products generated by forced decomposition of samples were also investigated for interference with the analytical method. Stress conditions, such as: thermal degradation, photolysis and oxidation test, acidic and alkaline conditions were applied to standard and sample solutions. Peak purity test (photodiode array detector) was useful to show that the chromatographic peak of the analyte did not contain impurities.
Results and Discussion: The best conditions were selected based on peak performance and the run time of the proposed assay was 10 min under isocratic elution. During injection of a standard solution the retention time was about 7.5 minutes for milnacipran hydrochloride. The chromatographic analysis under different analytical conditions (robustness) was performed and the chromatographic parameters of the main peak were evaluated presenting only few changes. The linear dynamic range was 20 – 100 $\mu g{\cdot}mL^{-1}$ ($R^2 \geq 0.999$). The validation data showed that LC method is reproducible, providing an accurate and precise quantitation of milnacipran in capsules. The chromatograms showed absence of any peak due to inactive ingredients and showed suitable separation from potential degradation products. The most important effect of degradation studies occurred by effect of photolysis at 254 nm and oxidation condition. In forced degradation study, the LC method was employed to analyze the assay and purity of samples subjected to degradation. The results showed levels of the drug decreased significantly and the presence of its degradation products. The kinetics of reaction after the photodegradation of milnacipran hydrochloride was determined.
Conclusions: The absence of official methods to quantify milnacipran hydrochloride justifies the need of analytical procedures for assuring the quality of its pharmaceutical dosage form. The LC method developed and validated allows a simple and fast quantitative determination of milnacipran hydrochloride in capsules, ensuring that it is suitable for determining the content of drug in this dosage form despite the presence of its major degradation products.
References:
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