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MIANSERIN HYDROCHLORIDE IN COATED TABLETS: STABILITY-INDICATING LIQUID CHROMATOGRAPHY METHOD AND PHOTODEGRADATION KINETICS STUDY

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Introduction: Mianserin hydrochloride is a drug for the treatment of depressive illness and depression associated with anxiety. Its antidepressant effect is mainly attributed to presynaptic alfa2-adrenoreceptor blocking activity and to serotonin receptors antagonism. Mianserin is classified as an atypical antidepressant, based on its mechanism of action not defined. In Brazil, mianserin coated tablets is available in the market as Tolvon®, commercialized by the Pharmaceutical Industry Organon. The lack of reliable methods for the quality assessment of pharmaceutical products limits the efficiency of the validation programs and monitoring of the same. Thus, only the validation of analytical methods, used to verify the quality of drugs, ensures that they meet the requirements of analytical applications.
Objective: The aim of this study is to develop and validate a stability-indicating LC method in compliance with the ICH Guideline for the determination of mianserin hydrochloride in coated tablets as well as to determine the photodegradation kinetics of the drug in methanolic solution.
Materials and Methods: Mianserin hydrochloride standard (99.90%) was kindly supplied by Pharmaceutical Industry Organon (São Paulo, Brazil) and the commercial tablets Tolvon® was obtained in the local market. Purified water was obtained by a Millipore® Direct-Q 3UV with pump. HPLC grade methanol, sodium hydroxide, hydrochloric acid, triethylamine, hydrogen peroxide and potassium monobasic phosphate (reagent grade) were purchased from Merck. The HPLC system (Agilent 1200 series, Santa Clara, USA) consisted of a diode array detector set at 278nm. Chromatographic analyses were performed in an Ace RP-18 octadecyl silane column (250mmx4.6mm i.d., particle size 5 µm) maintained at ambient temperature (25 ºC). The mobile phase was composed of methanol, 50 mM potassium monobasic phosphate buffer and a solution of triethylamine 0.3% adjusted to pH 7.0 with phosphoric acid 10% (85:15, v/v) in isocratic mode at a flow rate of 1 mL/min and the sample injection volume was 20 µL. The photodegradation kinetics was carried out with quartz cells containing mianserin hydrochloride in methanolic solution exposed to UVC radiation (254 nm), at pre-established times (0, 15, 30, 90, 120, 150 and 180 minutes).
Results and Discussion: The following analytical parameters were analyzed: specificity, linearity, precision, accuracy and robustness. In forced degradation studies, the effects of acid, base, oxidation, UV light and temperature were investigated showing no interference in the mianserin elution. Also, the formulation excipients did not interfere, demonstrating the specificity of the method. It was linear (r = 0.9999) at concentrations ranging from 50.0 to 110.0 µg/ml. The low values of relative standard deviations (RSD) for the repeatability (0.39%, 0.44% and 0.23%) and intermediate precision (0.83%) demonstrated adequate precision of the analytical method. The mean recovery data were 102.16%, satisfying the accuracy of the method. The method was robust and the LD and LQ was 0.21 and 1.05 µg/ml respectively. Submitting the drug to several factors, the light was the most sensitive. The mianserin photodegradation kinetic rate was determined by plotting the drug concentration (zero-order process), the log (first-order process) and the reciprocal (second-order process) concentration versus time. The degradation of mianserin in methanolic solutions could be better described as zero order kinetic (r = 0.9982).
Conclusions: The reverse phase LC method proposed was found to be simple, fast, accurate, precise, linear, robust and specific. The validated method may be used to quantify mianserin in coated tablets and to determine the stability of the drug. The method is able to separate mianserin from its degradation products and tablets excipients.

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