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HPLC determination of glibenclamide and its two impurities

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There is growing concern about the level of impurities and degradation products in pharmaceuticals and their possible implications in adverse reactions (Boehlert, 1997). Consequently interest is now focused on the development and validation of sensitive and selective analytical methods for determination of impurities in bulk powder and dosage forms. Glibenclamide is a sulphonylurea antidiabetic drug. It contains two impurities ; methyl N-4-[2-(5-chloro-2-methoxy benzamido) ethyl] benzene sulphonylcarbamate (impurity I) and 4-[2-(5-chloro-2-methoxy benzamido) ethyl] benzene sulphonamide (impurity II). A TLC test is specified in the British Pharmacopoeia for the semi-quantitative determination of the two impurities in glibenclamide raw material and tablets. The procedure involves an extraction step and evaporation to dryness at a temperature not exceeding 40^0 at a pressure of 2 kPa. The method is time-consuming and suffers from degradation of glibenclamide in the solvent mixture (methanol-chloroform) used in the test (Poirier et al. 1980). The present study describes a rapid and sensitive reversed-phase HPLC method for the simultaneous determination of glibenclamide and its two impurities (I) and (II) within 10 min. The chromatographic conditions adopted consist of the use of C_8 column (125 x 4 mm ID) packed with 5 μm particles and a mobile phase composed of an aqueous solution of 0.52% w/v ammonium dihydrogen phosphate and acetonitrile (50:50) with a final pH value of 5.4±0.1. The mobile phase was pumped isocratically at a flow rate of 0.6 ml/min. The eluate was monitored at 225 nm for the two impurities and at 300 nm for glibenclamide. Retention times were 3.7 min (impurity I) , 4.6 min (impurity II) and 8.2 min (glibenclamide). The proposed method was validated according to current guidelines for linearity, precision, accuracy and limits of quantitation for the two impurities. The method was applied to the determination of glibenclamide and its two impurities in batches of raw material and glibenclamide tablets.

The results of analysis of four batches of glibenclamide raw material showed that the levels of impurity (I) ranged between 0.24 and 0.43%. For impurity (II) the levels ranged between 0.10 and 0.93%. The glibenclamide contents of the four batches were within 99-101%. For the brands of glibenclamide tablets examined, the levels of carbamate impurity (I) did not exceed 0.31%. However, the level of sulphonamide impurity (II) showed a significant increase in some brands reaching 3.79% i.e. above the limit specified by BP (2.4%). This is possibly due to hydrolysis during storage (Wiseman et al. 1964). The suggested HPLC method is suitable for purity assessment of glibenclamide raw material and monitoring stability of glibenclamide in tablets. The method couples both simplicity and sensitivity. Limit of quantitation is 5 ng for both impurities compared to 1 μg for the TLC procedure of the BP (Poirier et al. 1980).

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