Development and Validation of Analytical Method for Simultaneous Estimation of Timolol Maleate and Hydrochlorothiazide in Bulk and In Their Tablet Dosage Form

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ABSTRACT

A simple, accurate and precise reverse phase high pressure liquid chromatography (RP-HPLC) method was developed and validated for simultaneous estimation of Timolol Maleate and Hydrochlorothiazide in bulk and in their tablet dosage form. The RP-HPLC method has shown adequate separation for Timolol Maleate and Hydrochlorothiazide from its degradation products. The separation was achieved on a Hypersil BDS C_{18} (250mm X 4.6mm i.d., 5µm particle size) with an isocratic mixture of water : Methanol : Triethyleamine pH 3.5 adjusted with phosphoric acid in the ratio of 15:85:0.25 v/v. The mobile phase at a flow rate of 1.0ml/min in isocractic mode, injection volume 20µl and wavelength of detection was kept at 293nm. Timolol Maleate and Hydrochlorothiazide was retained at 2.280±0.1min and 4.283±0.1min, respectively. The linearity of the proposed method was investigated in the range

of 5-15µg/ml and 12.5-37.5µg/ml for Timolol Maleate and Hydrochlorothiazide, respectively. Correlation coefficient was 0.997 and 0.998 for Timolol Maleate and Hydrochlorothiazide, respectively. The limit of detection was 0.82µg/ml and 1.67µg/ml for Timolol Maleate and Hydrochlorothiazide, respectively and the limit of quantification was 2.51µg/ml and 5.08µg/ml for Timolol Maleate and Hydrochlorothiazide, respectively. Force degradation study was carried out on combined dosage form as per ICH guideline and it was exposed to hydrolysis (acid and base hydrolysis), oxidative and thermal conditions to apply stress. Proposed methods were validated as per ICH guidelines for linearity, accuracy, precision, and robustness, and for estimation of Timolol Maleate and Hydrochlorothiazide in commercially available tablet dosage form and results were found to be satisfactory. Thus the developed and validated stability indicating method can be used successfully for marketed formulations.

Key words: Timolol Maleate, Hydrochlorothiazide, RP-HPLC method, Force degradation