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Determination of Metoprolol Tartrate by Reverse Phase HPLC

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A simple, precise and accurate reverse phase high performance liquid chromatographic method has been developed for the determination of metoprolol tartrate in pharmaceutical formulations. An ODS C_{18} (25 cm X 4.6 mm) column from Shimadzu in isocratic mode, with mobile phase acetonitrile:methanol:0.5 % glacial acetic acid in triple distilled water:triethylamine (56:18:26:0.1v/v) was used. The flow rate was 1 ml/min and effluent was monitored at 280 nm. Betaxolol hydrochloride was used as the internal standard. The retention times were 4.6 mm and 5.8 mm for metoprolol tartrate and betaxolol hydrochloride respectively. The linearity range was found to be 0.1-40 μg/ml.

Metoprolol tartrate[1] (MT) is a β-adrenoreceptor blocking agent used in the management of angina pectoris, cardiac arrhythmia and hypertension. Chemically it is known as 1-[4-(2-methoxyethyl)phenoxy]-3-(1-methylethylamino)-2-propanol and is official in USP[2] and IP[3]. Several analytical methods such as non-aqueous titration[2,3], spectrophotometry[3,4], potentiometry[5], spectrofluorimetry[6], TLC[7], GC[8] and HPLC[2,9-19] for bulk and pharmaceutical dosage forms and in biological fluids have been reported in literature for its determination.

Tablets, capsules and injections, available in local market, were procured and were analysed for MT content by new RP-HPLC method which was found to be simple, precise, rapid and selective. This method obeys linearity in the concentration range of 0.1-40 μg/ml.

Shimadzu HPLC, LC-10AT solvent delivery module with UV/Vis spectrophotometric detector Shimadzu SPD-10A was used. Afcoset ER-200A electronic balance was used for weighing the samples. Reference standard of betaxolol hydrochloride and metoprolol tartrate are procured from M/s Cipla Laboratories, Mumbai. Acetonitrile HPLC grade and glacial acetic acid AR grade were procured from E. Merck (India) Ltd. Mumbai. HPLC grade methanol from Mallinckrodt Baker, Inc, Paris, Kentucky and triethylamine AR grade from Ranbaxy Ltd., S.A.S. Nagar, were procured and used.

For the preparation of stock solution of internal standard and metoprolol tartrate, 50 mg of each drug was weighed and dissolved in water separately and diluted upto 50 ml with triple distilled water. An aliquot (2.5 ml) was pipetted out from this stock solution of BX and made upto 25 ml with mobile phase. MT (1 ml) was diluted to 50 ml with mobile phase. In order to prepare test sample solutions, the

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drug present in formulations was extracted into the mobile phase and estimated.

The procedure for calibration and assay was as follows. Aliquots of working standard solution of MT in the range of 0.1-40 µg/ml were taken in different 10 ml graduated test tubes, 1 ml of 20 µg/ml of BX as internal standard was added to all the graduated tubes and diluted upto the mark with mobile phase. Standard and sample solutions (20 µl) were injected into the injector of HPLC system. It was ensured that the peaks of BX and MT are well separated. The peak areas were recorded with UV detector at 280 nm. The ratios of peak area of drug to the internal standard were plotted against concentration in µg/ml. Each solution was run thrice at an interval of 10 min to ensure elution of earlier injection. The amount of MT present in formulations was compared from calibration curve.

The proposed chromatographic conditions ascertain resolution and reproducibility, system suitability tests were carried out on freshly prepared standard stock solution of MT and IS and the parameters obtained such as limit of detection (LOD), limit of quantitation (LOQ), relative retention time of drug with respect to IS, tailing factor and resolution are showm in Table 2. The plot ratio of area of MT to the area of IS Vs concentration of MT is found to be linear in the range of 0.1 to 40 µg/ml with coefficient of correlation (r=0.94). The optimum mobile phase acetonitrile:methanol:0.5 % glacial acetic acid in TD waters:triethylamine (56:18:26:0.lv/v) is selected because

TABLE 1: RESULTS OF ANALYSIS OF FORMULATIONS.

Formulations	Amount claimed (mg)	Amount found (mg)	% RSD (n=6)
Tablets			
Brand-I	50	49.6	0.625
Brand-II	100	99.8	0.427
Capsules			
Brand-I	25	24.91	0.516
Injection			
Brand-I (mg/ml)	1	0.982	0.389

The tablets employed were, brand I- Betaloc 50 mg (Astra IDL), brand II- Metolar 100 mg (Cipla). The capsules employed were, brand I- Betaloc 25 mg (Astra IDL) and the injection brand I were Metolon 1 mg/ml (Cipla).

it is found to ideally resolve the peaks of both BX and MT at the retention times 4.6 and 5.8 min, respectively.

To study the accuracy, reproducibility and precision of the proposed method, recovery experiments were carried out. A fixed amount of preanalyzed sample was taken and standard drug was added at three different concentration levels (75, 100 and 125%), recovery studies gave results between 99.82 to 100.15%. The amount of MT present in pharmaceutical dosage forms found by the proposed method is shown in Table 1. The low values of RSD indicate the method is precise and accurate. The proposed method gives good resolution between MT and IS within short analysis time (<7.0 min). The method is very simple, rapid and highly precise. High percentage of recovery shows that the method is free from interferences of the excipients used in the formulations. Therefore the method can be useful in routine quality control analysis of metoprolol tartrate.

TABLE 2: RESULTS OF LINEARITY AND SYSTEM SUITABILITY.

Parameters	Metoprolol tartrate
Linearity range (µg/ml)	0.1-40
LOD (µg/ml)	0.07
LOQ (µg/ml)	0.05
Tailing factor	1.15
Resolution between MT and IS	0.869
Relative retention time (min)	0.79

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A Colorimetric Assay Method for Nabumetone

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A simple spectrophotometric method has been developed for the estimation of nabumetone in pure and pharmaceutical dosage forms. In this method, the drug is made to react with ferric chloride and 1,10-phenanthroline when a red complex is formed. The chromogen can be estimated at 517 nm against a reagent blank. The method obeys Beer's law in the concentration range of 1-5 μg/ml of the drug.

Nabumetone[1] (4-(6-methoxy-2-naphthalenyl)-2-butanone) is a non-steroid anti-inflammatory drug mainly used in the treatment of rheumatoid and osteoarthritis[2]. So far, a few HPLC[3,4] and colorimetric[5] methods have been reported for the assay of nabumetone in pure and various dosage forms. The authors describe a new sensitive colorimetric method for the assay of the drug.

All the chemicals used in the assay were of analytical grade. Solutions of ferric chloride (0.9%) and 1,10-phenanthroline (0.1 M) were prepared in distilled water. Spectral and absorbance measurements were made on a Systronics UV/vis spectrophotometer. An appropriate amount of nabumetone was accurately weighed and dissolved in 100

ml of methanol to obtain a working standard solution of 50 μg/ml.

Aliquots of the working standard solution ranging from 0.2-1.0 ml were transferred into a series of 10-ml of volumetric flasks. To each of the flasks, 0.5 ml of ferric chloride and 1.5 ml of 1,10-phenanthroline solutions were successively added and the final volume was brought to 10 ml with methanol. The absorbance of the blood red colored species obtained in each tube was measured at 517 nm against a reagent blank and the corresponding calibration curve was plotted. The optical characteristics for the method were calculated and the values obtained are summarized in Table 1. For the determination of the drug in tablets by the above method, the sample solution was prepared by extracting appropriate amount of the powder of the tablets of Nabuflam of M/s Microlabs Ltd. (each containing 500 mg of

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