Based on the above results and the statistical analysis[5] of dissolution data using ANOVA and 't' test, the best coat was selected. The 't' test was carried out only if ANOVA was significant at 5% level. Statistical analysis had showed that for the 400 ml coats, the difference in the dissolution rate (Table 4) at 60 min between 4% and 6% w/v solutions was insignificant at 5% level. But, 400 ml coat of 6% w/v solution were considered as the best since 400 ml coat of 4% w/v solution was dilute and took long time to dry during coating. Thus, drying time was also taken into consideration while choosing the best coating formula. Even though the tablets coated with 400 ml of 8% w/v solution had just passed (approximately 87%) the USP dissolution requirements [85% (Q)] in 60 min, it is not recommended to use this concentration for coating as the value is on the border. In the light of the above results, aqueous film coating with sodium alginate can be employed for cost effectiveness and competitiveness especially for export markets in addition to the associated safety. The 400 ml coat of 6% w/v aqueous film coating formula, which was chosen as the best, could be used for coating any extremely unpalatable tablets in addition to metronidazole tablets.

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A New Reverse Phase High Performance Liquid Chromatographic Method for Analysis of Rofecoxib in Tablets

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Accepted 3 November 2003

Revised 18 August 2003

Received 12 August 2002

A simple, selective, rapid, precise and economical reverse phase HPLC method has been developed for the determination of rofecoxib in tablets. The analyte is resolved by using a mobile phase (methanol and water in the ratio 50:50) at a flow rate of 1 ml/min on an isocratic HPLC system (Shimadzu) consisting of LC 10AT liquid pump, SPD 10A UV-Visible detector, a ODS C-18 RP column (4.6 mm I.DX25 cm) at a wavelength of 230 nm. The linear dynamic range for rofecoxib was 2-40 μg/ml by this method. Paracetamol was used as an internal standard.

Rofecoxib is a new non-steroidal antiinflammatory drug. It is commonly prescribed in the treatment of osteoarthritis and chemically it is 4-[4-(methyl sulfonyl) phenyl]-3-phenyl-2 (5H)-furanone[1]. A survey of literature reveals that two HPLC methods[2-3] are reported for the determination of rofecoxib in biological fluids and in tablets[4]. In the present investigation, a new RPHPLC method is reported for the

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estimation rofecoxib from tablet dosage form.

An isocratic HPLC system (Shimadzu) consisting of LC 10 AT liquid pump, SPD-10A UV visible detector, a ODS C-18 RP column (4.6 mm I.Dx25 cm) 25 µl Hamilton injecting syringe and window based single channel software was used. Afcoset electronic balance was used for weighing the materials. Pure samples of rofecoxib and paracetamol were procured from M/s Cipla Labs, Mumbai and Dr. Reddy's laboratories, Hyderabad. Methanol and acetonitrile used were of HPLC grade and obtained from E. Merck (India) Ltd., Mumbai. Water used was of triple distilled prepared by all glass distillation apparatus. Optimized chromatographic conditions were shown in Table 1.

Standard stock solution rofecoxib was prepared by dissolving 25 mg of drug in 25 ml of acetonitrile to get 1 mg/ml solution and this solution was suitably diluted with mobile phase (methanol and water in the ratio 50:50) to get stock solution of concentration 10 µg/ml and 100 µg/ml. Stock solution of paracetamol (IS) was prepared by dissolving 25 mg of drug in 25 ml of mobile phase to get 1 mg/ml solution and was diluted to get a solution of concentration 5 µg/ml. Working standard solutions containing rofecoxib in various concentrations and paracetamol in the concentration of 5 µg/ml were prepared in the mobile phase as per the Table 2. Twenty microlitres of each solution was injected to HPLC system to obtain the chromatogram. The ratios of AUC of rofecoxib to IS were calculated and the results are shown in Table 2. The method follows the regression equation Y=0.1375X+0.053 with a coefficient of correlation (r=0.999).

TABLE 1: OPTIMIZED CHROMATOGRAPHIC CONDITIONS

Parameter	Optimized condition
Chromatograph	Shimadzu HPLC model LC-10AT
Mobile phase	Methanol: water (50:50)
Column	ODS C-18 RP (4.6 mm i.d.x25 cm
Flow rate	1.0 ml/min
Detection	UV at 230 nm
Injection volume	20 µl
Temperature	Ambient
Retention time-rofecoxib	7.79-8.00 min
Retention time-paracetamol, IS	3.42-3.49 min
Run time	11 min

Twenty tablets of rofecoxib were weighed, powdered and the powder equivalent to 25 mg was weighed accurately and taken into 25 ml volumetric flask. Rofecoxib was extracted in acetonitrile and the volume was adjusted to 25 ml, mixed and filtered. From the filterate, 0.1 ml was pipetted to 10 ml graduated test tube and spiked with required aliquot of IS solution and then volume was adjusted to 10 ml with the mobile phase such that the concentration of IS was 5 µg/ml. 20 µl of this solution was injected into HPLC system to obtain a chromatogram and the concentration of rofecoxib corresponding to the ratio of AUC of rofecoxib and AUC of IS in the formulations were calculated from the standard graph. The results are given in Table 3.

The proposed chromatographic conditions ascertain resolution and reproducibility, system suitability tests were carried out on freshly prepared standard stock solution of rofecoxib and IS and the parameters obtained such as limit of detection (LOD), limit of quantitation (LOQ), theoretical plates, tailing factor and resolution are shown in Table 4. The plot ratio of area of rofecoxib to the area of IS Vs concentration of rofecoxib is found to be linear in the range of 2.0-40.0 µg/ml with coefficient of correlation (r=0.999).The optimum mobile phase methanol:water (50:50 v/v) is selected because it is found to ideally resolve the peaks of both rofecoxib and IS at the retention times 8.0 and 3.49 min, respectively.

To study the accuracy, reproducibility and precision of the proposed method, recovery experiments were carried

TABLE 2: STANDARD GRAPH FOR THE ESTIMATION OF ROFECOXIB

Concentration (µg/ml)		Ratio of AUC of
Rofecoxib	Paracetamol (I.S)	rofecoxib to I.S.
2.0	5	0.37
5.0	5	0.74
10.0	5	1.42
20.0	5	2.80
30.0	5	4.08
40.0	5	5.64

All values are averages of three determinations.

TABLE 3: RESULTS OF ANALYSIS OF TABLETS CONTAINING ROFECOXIB AND RECOVERY STUDIES

PHARMACEUTICAL Formulation	Amount of rofecoxib (mg)		Percentage recovery
	Labelled	Found	
Tablet1 (TOROXX)	50	49.8	99.8
Tablet 2 (ROFIBAX)	25	24.9	98.4

Toroxx (Torrent) and Rofibax (Ranbaxy) are branded formulation. All values are average of three determinations.

TABLE 4: RESULTS OF LINEARITY AND SYSTEM SUITABILITY

Parameters	Rofecoxib
Calibration range (μg/ml)	2.0-40.0
LOD(μg/ml)	0.1992
LOQ (μg/ml)	0.664
Theoretical plates	1359
Tailing factor	1.041
Resolution: Between the peaks of I.S. and rofecoxib	2.24.

LOD is the limit of detection, LOQ is the limit of quantitation and IS is the internal standard.

out. A fixed amount of preanalyzed sample was taken and standard drug was added, recovery studies gave results between 98.44 to 99.75%.

The extracts of the formulation containing rofecoxib showed no significant peaks which indicates that the excipients in the solid dosage form are not interference in the estimation by this method and therefore this method is found to be specific.

The values of recovery studies indicates that the method is accurate. As the mobile phase is only a mixture of methanol and water, the run time is only 11 min and the flow rate is 1.0 ml/min the method is rapid and economical.

ACKNOWLEDGEMENTS

The authors are grateful to M/s Cipla Labs., Mumbai, and Dr. Reddy's Labs., Hyderabad for providing gift samples of rofecoxib and paracetamol. The authors are thankful to Roland Institute of Pharmaceutical Sciences, Berhampur for providing facilities.

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