Spectrophotometric Estimation of Rofecoxib in Tablet Dosage Forms

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A simple, accurate and sensitive spectrophotometric method has been developed for the estimation of rofecoxib in commercial preparations. The lactone ring in the drug is converted to hydroxy acid by sodium carbonate. 1,4-Napthoquinosulphonic acid acts as oxidizing agent and abstracts hydrogen ion from the hydroxy acid to form brown colored chromogen measured at the wavelength of maximum absorption 440 nm against reagent blank. The chromogen obeyed linearity over 20 to 120 µg/ml (r=0.9998). The method is satisfactorily applied for the analysis of pharmaceutical preparations containing rofecoxib. The results of the analysis were validated statistically and by recovery studies. The recovery ranged between 98.6 and 101.8 %.

Non-steroidal antiinflammatory drugs (NSAIDs) are used in the treatment of various inflammatory diseases and pain. NSAIDs produce their pharmacological and unwanted side effects by inhibiting cyclooxygenase (COX)–II and –I, respectively[1]. Recently introduced NSAIDs, celecoxib and rofecoxib, selectively inhibit COX-II and hence cause little or no gastrointestinal side effects[2]. Chemically rofecoxib is 4-[4-(methylsulfonyl)phenyl]-3-phenyl-2(5H)-furanone. So far, only HPLC assays have been reported for quantitation of rofecoxib in rat[3] and human plasma[3-5]. However, no colorimetric method has been reported for estimating rofecoxib in commercial preparations. Literature survey reports formation of stilbene-phenanthrene like photocyclization of rofecoxib on UV exposure forming fluorescent species[4]. The present work describes a simple colorimetric method for the estimation of rofecoxib in commercial preparations. The estimation is based on the conversion of lactone ring in the drug to hydroxy acid by sodium carbonate. NQSA acts as oxidizing agent and abstracts hydrogen ion from the hydroxy acid to probably form brown colored chromogen measured at 440 nm against reagent blank. The proposed method is simple and suitable for routine determination of rofecoxib in commercial preparations. This method also provides less time consuming, sensitive and economic procedure.

A GBC UV/Vis 911A spectrophotometer with 1 cm-matched cuvettes was used for spectrophotometric measurements. Gift sample of rofecoxib was received from Ranbaxy Limited, Indrad. Tablets of rofecoxib, Rofexib, Rofibax and Rofix (12.5 and 25 mg) were procured from a local pharmacy. NQSA solution (0.1%, Loba Chemie, Mumbai) and 3% sodium carbonate solution were freshly prepared in distilled water. The standard stock solution of rofecoxib (1 mg/ml) was prepared in 100 ml of 1:1 dioxane water system. The sample solution was prepared by extracting accurately weighed tablet powder equivalent to 100 mg of rofecoxib with 1:1 dioxane water system and filtered through whatman filter paper no. 40. The residue was washed with small volumes of solvent and the final volume was made up to 100 ml (1000 µg/ml).

The effect of NQSA reagent concentration on colour intensity was determined by transferring 1 ml of standard solution to ten separate volumetric flasks, in which 0.5 to 5.0 ml of NQSA and 1 ml of sodium carbonate solutions were added. The solution is heated on boiling water bath for 5 min, cooled at room temperature and set aside for 15

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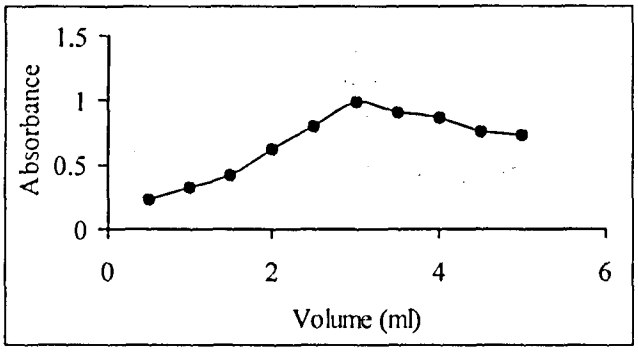

Fig. 1: Effect of NQSA reagent concentration on color intensity.

The optimized quantity of NQSA (0.1%) was 3 ml. The optimization was carried over the range of 0.5 to 5.0 ml of standard NQSA solution.

min for reaction to complete. The volume of each flask was adjusted to 10 ml with distilled water and the absorbance was measured at 440 nm against reagent blank (fig.1).

The effect of sodium carbonate reagent concentration on color intensity was tested by transferrinig 1 ml of standard solution to ten separate volumetric flasks in which 3 ml of NQSA reagent and 0.1 to 1.0 ml of sodium carbonate solution were added. The solution was heated on boiling water bath for 5 min, cooled at room temperature and set aside for 15 min. The volume of each flask was adjusted to 10 ml with distilled water and the absorbance was measured at 440 nm against reagent blank (fig. 2). The brown colored compound (probably chromogen) was prepared as mentioned above with 3.0 ml of NQSA and 0.5 ml of sodium carbonate for stability study. The absorbance was measured

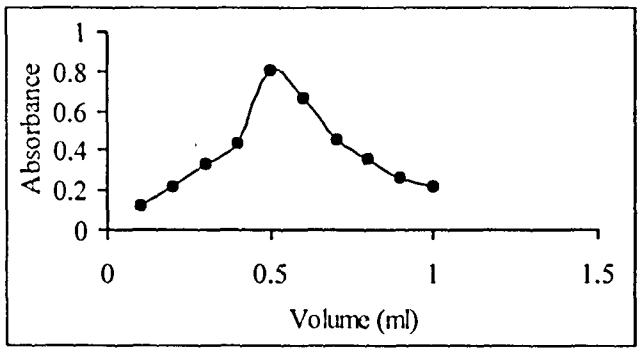

Fig. 2: Effect of Na_2CO_3 concentration on color intensity.

The optimized quantity of Na_2CO_3 (3%) was 0.5 ml. The optimization was carried over the range of 0.1 to 1.0 ml of standard Na_2CO_3 solution.

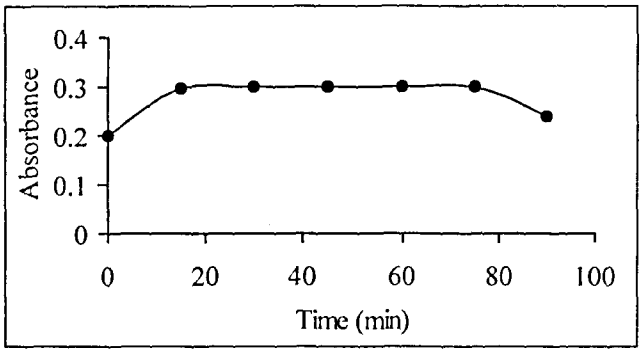

Fig. 3: Stability curve.

The stability of the chromogen prepared with 3.0 ml of NQSA and 0.5 ml of sodium carbonate was measured at 440 nm at the interval of 15 min for 1.5 h with stability of 60 min.

at 440 nm at the interval of 15 min for 1.5 h (fig. 3).

Aliquots of 0.2 ml to 1.2 ml portion of standard solution were transferred to series of 10 volumetric flasks. To each flask 3.0 ml of NQSA and 0.5 ml of sodium carbonate were added. The solution was heated on boiling water bath for 5 min, cooled at room temperature and set aside for 15 min for reaction to complete. The volume of each flask was adjusted to 10 ml with distilled water and the absorbance was measured at 440 nm against reagent blank. The calibration curve was constructed. Similarly the absorbance of sample solution was measured and the amount of rofecoxib was determined by referring to the calibration curve.

To test the accuracy and reproducibility of the proposed method, the recovery experiments were performed by adding known amount of drug to the pre-analyzed formulation and re-analyzing the mixture by proposed method (Table 1). The recovery was performed at 100, 200 and 300 % levels. Study was carried out to test the ruggedness of the method through an interday and intraday day analysis of three batches of rofecoxib tablets. Each batch was analyzed twice a day for three days.

The lactone ring in rofecoxib is converted to hydroxy acid by sodium carbonate. NQSA acts as oxidizing agent and abstracts hydrogen ion from the hydroxy acid and forms probably the brown colored chromogen measured at the wavelength of maximum absorption 440 nm against reagent blank. It was found that 3 ml of NQSA and 0.5 ml of sodium carbonate were necessary for the achievement of maximum color intensity. However the absorbance decreased with higher and lower amounts of NQSA reagent and so-

TABLE 1: ANALYSIS OF ROFECOXIB SAMPLES

Formulation	Label claim (mg)	Percent estimated*	Percent recovery*
Tablet 1	12.5	98.5	98.7
	25.0	100.0	101.8
Tablet 2	12.5	100.2	101.0
	25.0	100.3	99.0
Tablet 3	12.5	99.1	99.4
	25.0	100.5	98.7

*Mean of five determinations. Tablet 1, Tablet 2 and Tablet 3 stand for Rofexib, Rofibax and Rofix each containing 12.5 and 25 mg of rofecoxib

dium carbonate solution (figs. 1 and 2). It was found that 15 min are required to complete the reaction i.e. to form the stable brown compound probably chromogen. The brown color was stable for further 60 min (fig. 3).

Pure rofecoxib spiked with common excipients such as starch, talc, lactose and magnesium stearate was assayed and it was found that the assay result was unaffected by the presence of such excipients. In the rofecoxib tablet it was noticed that the excipients did not interfere in the absorbance.

The calibration curve yielded coefficient of correlation (r) 0.9998 over the Beer's range of 20 to 120 µg/ml. The regression equation for rofecoxib was found to be

TABLE 2: STATISTICAL ANALYSIS OF RESULTS FOR ROFECOXIB

Formulation	Label claim (mg)	Standard deviation	Coefficient of variation	Standard error	95% confidence interval
Tablet 1	12.5	0.8516	0.8648	0.3477	0.8939
	25.0	1.0478	1.0483	0.4278	1.0997
Tablet 2	12.5	0.9262	0.9248	0.3781	0.9721
	25.0	0.8444	0.8420	0.3447	0.8863
Tablet 3	12.5	0.7963	0.8034	0.3251	0.8358
	25.0	1.0279	1.0228	0.4197	1.0790

Statistical treatment of the assay results for rofecoxib tablets with 5 determinations. Tablet 1, Tablet 2 and Tablet 3 stand for Rofexib, Rofibax and Rofix each containing 12.5 and 25 mg of rofecoxib

TABLE 3: INTERDAY AND INTRADAY ANALYSIS FOR ROFECOXIB

Day	Time	Tablet 1	Tablet 2	Tablet 3
First Day	Morning	99.26	100.3	98.67
	Evening	98.93	100.8	98.57
Second Day	Morning	99.11	101.1	99.42
	Evening	98.31	100.2	98.34
Third Day	Morning	99.29	101.1	99.66
	Evening	100.2	101.4	99.45
Mean		99.18	100.8	99.02
SD		0.5802	0.4153	0.5089
% CV		0.5847	0.4120	0.5139

Confirmation of ruggedness of the analytical method by interday and intraday studies.

y=0.0076x+0.0005. The molar absorptivity and Sandell's sensitivity are 2.379×0^3 l/mol.cm and 0.1323 μg/cm²/0.001, respectively, which indicate sensitivity of the method. The percent coefficient of variation (% CV) calculated from five replicate readings (absorbance values) at concentration 80 μg/ml of rofecoxib was found to be 0.2818, which is less than 2% confirming precision of the method. In a replicate analysis (n=5) of three brands of rofecoxib tablets each of 12.5 mg and 25 mg by proposed method, the percentages of rofecoxib were found to be in the range of 98.48–100.51 (Table 1). The percentage recoveries were found to be in the range of 98.69 to 101.83 (Table 1), indicating non-interference from the formulation excipients. The low values of standard deviation, %CV and 95% confidence limit reveal that the assay method is accurate and precise (Table 2). Ruggedness of method was checked and confirmed by an interday and an intraday analysis (Table 3).

A new, simple and statistically validated colorimetric method using NQSA reagent has been developed for the quantitative determination of rofecoxib in tablet formulation. The main advantage of the proposed method is its suitability for the routine quality control of the drug alone and in tablets without interference caused by the excipients expected to be present in the tablets.

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REFERENCES

1. Cryer, B. and Feldman, M., **Amer. J. Med.,** 1998, 104, 413.
2. Bolten, W.W., **J. Rheumatol.** 1998, 51, 2.
3. Sattari, S. and Jamali, F., **J. Pharm. Pharm. Sci,** 2000, 3, 312.
4. Woolf, E., Fu, I. and Matuszewski, B., **J. Chromatogr. B.,** 1999, 730, 221.
5. Lalla, J.K., Hamrapurkar, P.D., Yadav, S.P. and Vyas, P.M., **Indian J. Pharm. Sci.,** 2004, 66, 338.

UV Spectrophotometric Determination of Carvedilol

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Two simple, fast, convenient, precise, reproducible UV spectrophotometric methods have been developed for the determination of carvedilol in pure form in tablets using methanol (method A) and polyethylene glycol-400:water (2:1) (method B). The UV spectrum of carvedilol showed absorption maxima at 242 nm and 245 nm, respectively in methanol and PEG-400:water (2:1). Good agreement with Beer's law was found in the range of 2 to 20 μg/ml for method A and 1 to 10 μg/ml for method B.

Carvedilol (CVD), (±)-1-(9H-carbazol-4-yloxy)-3-[(2-(2-methoxy phenoxy)] ethyl amino] -2-propanol[1], is a new antihypertensive drug, which has an additional α-adrenergic receptor antagonist activity and has been approved for the treatment of essential hypertension and symptomatic heart failure[2]. Literature survey revealed the availability of a HPLC method with spectrofluorometric detection[3] and Tandem mass spectrometric method[4] for its estimation. No reported UV Spectrophotometric methods are available for routine quality control analysis. The present paper describes two simple, reproducible and sensitive UV spectrophotometric methods for the determination of CVD.

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