solution of the dosage form spiked with mixture containing known amount of these two drugs. Each experiment was repeated five times and mean recovery and percentage coefficient of variation (% C.V.) are given in Table 3. As can be seen from the table, recovery values are all between 99.5 to 101% and % C.V. values of replicate estimation do not exceed 3 %. A simple, sensitive and rapid method has been developed for the isocratic separation and simultaneous estimation of metformin and glimepiride in bulk and pharmaceutical dosage forms by using wavelength programming in HPLC.

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Extractive Spectrophotometric Method for the Determination of Clarithromycin

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A simple extractive spectrophotometric method has been developed for the estimation of *clarithromycin in both pure and pharmaceutical dosage forms.* The method is based on the formation of an ion-pair complex of the drug with bromocresol green, which is extracted into chloroform. The absorbance of the chloroform layer is measured at 415 nm against a reagent blank. The method has been statistically evaluated.

Clarithromycin (CMN), 6-methoxy erythromycin[1,2] is used for the treatment of streptococcal pharyngitis, respiratory tract infections and acute sinusitis. It is currently being evaluated for the treatment of some refractory infections in AIDS patients[2]. A few analytical methods based on ion-pair HPLC[3], capillary electrophoresis[4] and RP- HPLC[5,6] to estimate the drug in gastric juice, plasma, serum and urine appeared in literature. Some HPLC[7,8] and colorimetric[9-13] methods have also been reported for the assay of CMN in various dosage forms and in bulk drugs. The authors report the development of a simpler extractive spectrophotometric method based on the formation of an ion-pair complex with bromocresol green (BCG) for its determination.

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A Systronics UV/Vis spectrophotometer (model 117) with 10 mm matched quartz cells was employed for all the spectral measurements. Chemicals used in the investigation were of analytical grade. The BCG solution (0.5%) was prepared by dissolving 500 mg of the dye in 100 ml of distilled water. This solution was shaken with chloroform to remove any chloroform soluble impurities. An accurately weighed quantity of clarithromycin (100 mg) was dissolved in 100 ml of methanol to obtain a stock solution of 1 mg/ml strength. This solution was further diluted with distilled water to get a working standard solution containing 100 μg/ml of the drug.

Aliquots of the standard drug solution ranging from 0.5-3.0 ml were transferred into a series of 150 ml separating funnels. To each funnel, 2 ml of HCl (0.1 N) and 1 ml of the dye solution were added and the total volume was adjusted

to 10 ml with distilled water. Chloroform (10 ml) was added to each separating funnel. The funnels were shaken well for thorough mixing of the two phases and were allowed to stand for clear separation of the layers. The absorbances of the separated chloroform layers were measured against the reagent blank at 415 nm and a calibration curve was drawn for the standard dilutions. The optical characteristics such as Beer's law limits, Sandell's sensitivity, molar extinction coefficient, percent relative standard deviation, (calculated from the eight measurements containing 3/4th of the amount of the upper Beer's law limits), percent range of error (at 0.05 to 0.01 confidence limits) were calculated for the method and the results are summarized in Table 1.

The proposed method was used for determination of the drug in its tablet form. Three different commercial samples of the drug tablets, Crixan (Crossland), Clarithro (Alembic) and Claric (Ind-Swift) were chosen for the purpose. A weighed quantity of the tablet powder (from 20 tablets) equivalent to 100 mg of CMN was shaken with 100 ml of methanol in a volumetric flask and filtered. Appropriate aliquots of this solution were taken and the above described assay procedure was adopted. The drug contents were found out using the standard calibration curve. The recovery values obtained for CMN in different tablet formulations by the proposed method have been compared with a reported method and presented in Table 2.

TABLE 1: OPTICAL CHARACTERISTICS AND PRECISION DATA.

Parameters	
Beer's law limit (μg/ml)	5.0-30.0
Molar absorptivity (l/mol/cm)	1.9347×10^4
Sandell's sensitivity (μg/cm^2/0.001 absorbance unit)	0.03865
Regression equation (Y=a+bC)*	
Slope (b)	0.0259
Intercept (a)	0.0018
Correlation coefficient (r)	0.9998
Relative standard deviation (%)	0.5806
% Range of error	
95% confidence limit	0.4855
99% confidence limit	0.7183

*where C is the concentration (μg/ml) and Y, the absorbance.

TABLE 2: DETERMINATION OF CMN IN TABLETS.

Sample (Tablets)	Labelled amount (mg)	Amount obtained (mg)		Percent recovery by the proposed method*
		Reported method[9]	Proposed method	
Crixan	250	249.6	250.0	99.99
Clarithro	250	250.0	250.1	100.0
Claric	250	249.8	250.0	99.98

*Average of six determinations.

Studies revealed that the common excipients and other additives usually present in the dosage form did not interfere in the proposed method. The proposed extractive spectrophotometric method appears to be simple, sensitive, and accurate enough for the determination of CMN from tablets.

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Spectrophotometric Method for Estimation of Some COX-2 Inhibitors in Pure form and in Pharmaceutical Formulations

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Ultraviolet absorption spectrophotometric method for the estimation of celecoxib, rofecoxib, meloxicam and nimesulide in pure form and in pharmaceutical formulations has been developed. The solvents employed were 10% (v/v) aqueous dimethylsulfoxide for rofecoxib, 10% (v/v) aqueous dimethylformamide for meloxicam, 20% (v/v) aqueous acetonitrile for celecoxib and nimesulide. 0.1 N sodium hydroxide was also used as solvent for all the drugs except rofecoxib. All the solvents were found to give accurate, sensitive and reproducible results for the estimation of drugs in pure form. These solvent systems could also be used for the estimation of drugs from solid formulations. For the estimation of drugs in pure form, method involving the use of 0.1 N sodium hydroxide was found to be relatively more precise, economical and safer than the one involving the use of organic solvents. For the estimation of celecoxib, rofecoxib and meloxicam from the formulations, on the other hand, the use of organic solvents gave better results and should be preferred. For the estimation of nimesulide from formulations, however, again 0.1 N sodium hydroxide was found to be a better solvent.

Nonsteroidal antiinflammatory drugs (NSAIDs), are the most widely used medications in the world. The adverse effects associated with traditional NSAIDs are primarily the result of the inhibition of prostaglandin synthesis by blocking the enzyme cyclooxygenase (cox) activity throughout the body. The new category of NSAIDs , the selective cox-2 inhibitors, has potential advantages over the traditional NSAIDs[1]. Four cox-2 inhibitors, celecoxib, rofecoxib, meloxicam and nimesulide have been selected for the present investigations. Spectrophotometric estimation of nimesulide has been reported by a number of workers using different solvents[2,3]. However, very few spectrophotometric[4-7] and other methods[8,9] are available for the estimation of rofecoxib, celecoxib and meloxicam. Moreover, none of the methods have reported the use of organic solvent-water mixtures with low concentrations of organic solvents. In the present paper, an attempt has been made to develop a quick, sensitive, economical and safer spectrophotometric method for the estimation of these drugs.

Rofecoxib and celecoxib were obtained as gift samples from M/s. Ranbaxy Research Laboratories, Gurgaon. Meloxicam and nimesulide were also gift samples from Ms. Sun Pharmaceutical Industries Ltd., Mumbai and Panacea Biotec Ltd., Lalru, respectively. All solvents were of analytical grade. They were first dried by keeping in contact with Linde type 4A molecular sieves overnight.

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