
Spectrophotometric Method for Simultaneous Estimation of Nimesulide and Diclofenac Sodium from Combined Dosage Form

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A simple, accurate and economical spectrophotometric method was developed for simultaneous estimation of nimesulide and diclofenac sodium in bulk drug and in combined formulations using simultaneous equation method. Nimesulide and diclofenac sodium has λ_{max} at 297 nm and 283 nm respectively in methanol, showing linearity in the concentration range of 5-40 $\mu\text{g/ml}$ and 2.5-25 $\mu\text{g/ml}$ respectively. The results of analysis have been validated statistically and recovery studies confirmed the accuracy of the proposed method.

Nimesulide¹ (NM) is a non-steroidal antiinflammatory drug and chemically, it is N-(4-nitro-2-phenoxyphenyl) methane sulfonamide. Diclofenac sodium² (DFS) is a non-steroidal antiinflammatory drug, analgesic and antipyretic agent with minimal side effects. Chemically it is sodium {2-(2,6-dichloroanilino) phenyl} acetate, which is official in IP² and BP³. The pharmacopoeias describe a non-aqueous titration method for the analysis of tablets of diclofenac sodium. A few spectrophotometric⁴⁻¹² methods for the analysis of nimesulide and spectrophotometric methods¹³⁻¹⁵ for the analysis of diclofenac sodium from their respective formulations have been reported. But there is no evidence in literature for simultaneous estimation of these drugs in combination products.

The combination of drugs are indicated for the treatment of acute painful inflammatory conditions associated with muscle spasms like lumbago, spondylitis, trauma, fractures and degenerative processes such as osteoarthritis, rheumatoid arthritis. Hence, in the present investigation, a simple, rapid and reproducible method was developed for simultaneous estimation of NM and DFS from their combined dosage forms.

Spectral and absorbance measurements were made on an Elico SL -159 UV/Vis spectrophotometer by using 1-cm quartz cells. Afcoset ER-200A electronic balance was used for weighing the samples. Gift samples of nimesulide and

diclofenac sodium were obtained from M/S Dr. Reddy's Laboratories, Hyderabad. Methanol used was of analytical grade and obtained from Merck India Ltd., Mumbai. Capsules of two different brands (Niap-D, Cipla Laboratories Ltd. and Emsulide-D, Emcure Laboratories Ltd.) containing 100 mg of NM and 50 mg of DFS were procured from the local market.

Standard stock solution was prepared by dissolving 25 mg of each in 25 ml of methanol to get a concentration of 1 mg/ml. From this, suitable dilutions were made with methanol to get working standard solutions of 100 $\mu\text{g/ml}$ and 50 $\mu\text{g/ml}$, respectively. To construct Beer's plot for NM and DFS, different aliquots of NM (0.5-4.0 ml, 1 ml=100 $\mu\text{g/ml}$) and DFS (0.5-5.0 ml, 1 ml=50 $\mu\text{g/ml}$) were taken and diluted with methanol to 10 ml. The absorbance was measured at 297 nm for NM and at 283 nm for DFS solutions against methanol. Fig. 1 represents the overlain spectra of both the drugs. Both these drugs obeyed linearity individually and in mixture within the concentration range of 5-40 $\mu\text{g/ml}$ for NM and 2.5-25 $\mu\text{g/ml}$ for DFS, respectively.

A solution containing known concentration of NM and DFS was prepared and the absorbance was measured at 297 nm and 283 nm. Based on the values E (1%, 1 cm) of NM (α_1, β_1) at 297 nm (λ_1) and DFS (α_2, β_2) at 283 nm (λ_2) were calculated. Then quantitative estimation of NM and DFS was carried out by solving the following simultaneous equations¹⁶. $X = \alpha_1 C_1 + \beta_1 C_2$, 297 nm $Y = \alpha_2 C_1 + \beta_2 C_2$, 283 nm where, C_1 and C_2 are the concentrations of NM and DFS respec-

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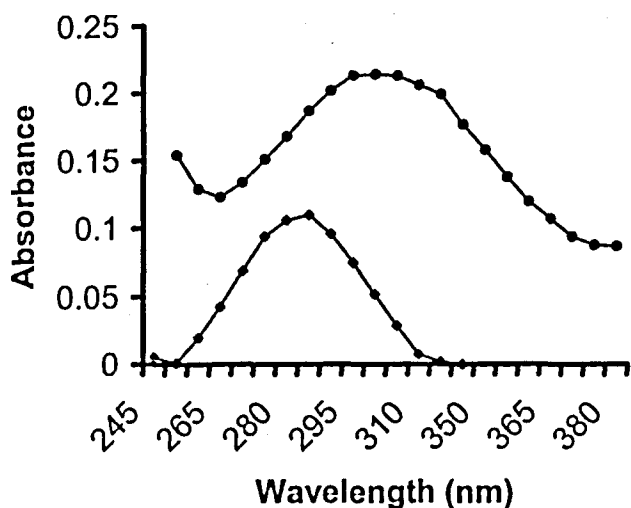


Fig. 1: Overlain spectra of nimesulide and diclofenac. Overlain spectra of nimesulide (NM, -●-) and diclofenac sodium (DFS, -◆-).

tively, X and Y are absorbance values at 297 nm and 283 nm, respectively and the values are of α_1 (217), β_1 (430), α_2 (187.5), β_2 (600).

Six replicates of five mixed standard solutions were prepared from standard stock solutions of the two drugs (Table 1). The absorbances of the solutions were measured at 297 nm and 283 nm for NM and DFS, respectively. Quantitative estimation of these drugs were carried out by solving the simultaneous equations.

For analysis of commercial formulations, twenty capsules were weighed. An accurately weighed quantity of powder equivalent to about 100 mg of NM was transferred into a 100 ml volumetric flask and dissolved in methanol. Then the solution was filtered and further diluted with methanol. Absorption values were recorded on spectrophotometer at 297 nm and 283 nm and were used to solve simultaneous equa-

TABLE 1: CONCENTRATIONS OF NIMESULIDE AND DICLOFENAC SODIUM IN MIXED STANDARD SOLUTIONS.

Nimesulide ($\mu\text{g/ml}$)	Diclofenac Sodium ($\mu\text{g/ml}$)
0.00	0.00
5.00	2.50
10.00	5.00
20.00	10.00
40.00	20.00
50.00	25.00

tions. The results are shown in Table 2.

The proposed method for simultaneous estimation of nimesulide and diclofenac sodium in combined dosage form was found to be simple, accurate, economical and rapid. Validation of the proposed method was carried out by performing recovery experiments, in which preanalysed samples were taken and standard drug was added at three different concentration levels. The results are shown in Table 3.

The validation parameters like percentage RSD, percentage range of error at 0.01 level, regression equation, slope, intercept and correlation coefficient were calculated and the results are shown in Table 4. The sensitivity of the proposed method was ascertained by Sandell's sensitivity, molar extinction coefficient and Beer's law range were also calculated and given in Table 4. The results reveal the suitability of the proposed method for simultaneous estimation of NM and DFS.

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TABLE 2: RESULTS OF ANALYSIS OF COMMERCIAL FORMULATIONS.

Formulations	Ingredient	Label claim (mg/capsule)	Amount found (mg/capsule)	% label claimed	SD
Capsules I (Nicip-D)	NM	100.0	99.97	99.97	0.28
	DFS	50.00	50.44	100.9	0.56
Capsules II (Emsulide-D)	NM	100.0	101.0	101.0	0.61
	DFS	50.00	49.60	99.20	0.56

NM: Nimesulide, DFS: Diclofenac Sodium, SD: Standard Deviation.

TABLE 3: RESULTS OF RECOVERY STUDIES.

Concentration of drug added to final dilution $\mu\text{g/ml}$		% of recovery	
NM	DFS	NM	DFS
5.0	2.5	099.8	99.5
10	5.0	099.6	99.7
20	10	100.0	99.4

NM: Nimesulide, DFS: Diclofenac Sodium.

diclofenac sodium. The authors are also grateful to Roland Institute of Pharmaceutical Sciences, Berhampur for providing the necessary facilities to carry out the research work.

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TABLE 4: VALIDATION AND SENSITIVITY OF THE PROPOSED METHOD.

Parameter	NM	DFS
λ_{max} (nm)	297	283
Beer's Law range ($\mu\text{g/ml}$)	5-50	2.5-25
Sandell's sensitivity ($\mu\text{g/cm}^2/0.001 \text{ AU}$)	0.0236	0.0110
Molar extinction coefficient	0.0131	0.0268
Regression equation		
Slope	0.0410	0.0839
Intercept	0.0385	0.0318
Correlation coefficient	0.9998	0.9999
% RSD	$\pm 4.53 \times 10^{-3}$	$\pm 3.49 \times 10^{-3}$
% range of error (0.01 level)	$\pm 5.60 \times 10^{-3}$	$\pm 4.31 \times 10^{-3}$

NM: Nimesulide, DFS: Diclofenac Sodium, RSD: Relative Standard Deviation, AU: Absorbance Unit.