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New Spectrophotometric Methods for the Determination of Nimesulide

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Two simple and sensitive spectrophotometric methods (A and B) in the visible region have been developed for the determination of nimesulide in bulk and in dosage forms. Method A is based on the reaction of reduced nimesulide with nitrous acid followed by its coupling with phloroglucinol to yield an yellow colored azo dye with an absorption maximum of 400 nm and method B is based on the reaction of reduced nimesulide with p-dimethylamino benzaldehyde (PDAB) to form an yellow colored chromogen wiht an absorption maximum of 415 nm.The color obeyed Beer's law in the concentration range of 4-20 µg/ml in method A and 4-24 µg/ml in method B.When pharmaceutical preparations (Tablets and suspension) were analysed, the results obtained by the proposed methods are in good agreement with the labelled amounts and are comparable with the results obtained by a reported mehtod. Recovery in both the methods is 98-101%.

Nimesulide[1] is a new non-steroidal antiinflammatory agent with minimal side effects. Chemically it is N-(4-nitro-2-phenoxyphenyl) methane sulfonamide. It is not yet official in any pharmacopoeia. A survey of the literature revealed that HPLC[2,3], HPTLC[4], non-aquenous titrimetric[5], polarographic[6] and very few spectrophotometric methods[7-10] were reported earlier for the estimation of nimesulide in biological fluids and in dosage forms. Pholoroglucinol and PDAB reagents were preferred by a number of workers[11,12] for visible spectrophotometric determination of drugs containing free or potenital primary arylamine. In the present investigation, the authors have developed two simple and sensitive spectrophotometric methods for nimesulide after converting it to its reduced form by zinc dust and hydrochloric acid[13]. The presence of primary aromatic amino group in the reduced nimesulide enable the use of diazotisation reaction with nitrous acid followed by coupling with pholoroglucinol (method A) to form an yellow colored azo dye[14] and condensation reaction with PDAB (Method B) to form a colored schiff's base. These reactions have not been reported earlier for the quantitation of nimesulide.

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EXPERIMENTAL

An ELICO Model SL-150 UV -VIS spectrophotometer with 1 cm matched quartz cells was used for all absorbance measurements. All the chemicals used were of Analar grade. Methanolic solution of PDAB (Qualigens; 0.1% w/v) and aqueous solutions of hydrochloric acid (Qualigens; 5 M), sodium nitrite (Qualigens; 0.1% w/v), ammonium sulfamate (Loba Chemie; 0.5% w/v) and pholoroglucinol (Loba Chemie; 0.5% w/v) were prepared in the usual way. Nimesulide was obtained as gift sample from a local industry (M/s. Siris Pvt. Ltd., Vijayawada). Freshly prepared PDAB and phloroglucinol solutions were employed.

Nimesulide (50 mg), was accurately weighed and dissolved in 20 ml of methanol and treated with 5 g of zinc dust and 4 ml of conc. hydrochloric acid. After keeping for 1 h at room temperature, the solution was filtered through cotton wool, and the residue was washed with 3 x 10 ml portions of methanol. The excess hydrochloric acid present in the filtrate was removed under vaccum and the total volume was brought to 100 ml with distilled

Table 1 - Optical Characteristics of Nimesulide using proposed Methods

Parameter	Method A	Method B
λ max (nm)	400	415
Beer's law limit (μg/ml)	4-20	4-24
Molar absorptivity	7.129×10^3	6.128×10^3
(Lit. $mole^{-1}$. cm^{-1})		
Sandell's sensitivity		
(μg/cm^2/0.001 absorbance Unit)	0.043	0.051
Regression Equation *		
Slope (b)	9.0×10^{-4}	3.9×10^{-3}
Intercept (a)	4.0×10^{-3}	2.8×10^{-3}
Relative standard deviation (%)**	1.62	1.21
% Range of Error (0.05 level)**	1.35	1.01

* Y = a+bX, where x is the concentration of reduced nimesulide in μg/ml and Y is the absorbance at the corresponding λmax.
** Average of six replicates.

water. Working standard solutions were obtained by appropriate dilution of the standard solution.

Method A

Into a series of 25 ml volumetric flasks, aliquots (0.5 - 2.5 ml) of reduced nimesulide solution (200 μg/ml) were taken. To each flask 2 ml hydrochloric acid and 3 ml sodium nitrite solution were added and kept aside for 10 min. Then 5 ml each of ammonium sulfamate and pholoroglucinol solutions were added to each flask at 3 min time interval and diltuted to the mark with distilled water. The absorbance was measured at 400 nm against a reagent blank after 30 minutes.

Method B

Aliquots (0.2-1.2 ml) of reduced nimesulide solution (100μg/ml) were transferred into a series of graduated test tubes. To each tube 1.5 ml of PDAB solution and 0.1 ml of hydrochloric acid were added and mixed. After 5 min the volume was made upto 5 ml with methanol and the absrobance of the yellow colored species was measured at 415 nm against the reagent blank.

Analysis of formulations

Tablet powder or suspension equivalent to 50 mg of nimesulide was transferred into a 100 ml volumetric flask and mixed with 20 ml methanol and the solution was made in the same manner as described above, which were then analysed using the above procedures. The amount of nimesulide was computed from the respective calibration curve.

Recovery experiments

Recovery experiments were performed by adding a known amount of the drug to previously analysed pharmaceutical preparations and also to various excipients used in formulations. The results are presented in Table-2.

RESULTS AND DISCUSSION

Beer's law limits, molar absorptivity, sandell's sensitivity, slope and intercept of regression analysis using least square method, precision and accuracy of the analysis of six replicate samples containing 3/4th of the amount

Table 2 - Analysis of Pharmaceutical Preparations using the proposed methods

Pharmaceutical Preparation/ Excipient	Labelled amount (mg/tablet or 5 ml of suspension)	Amount found* by			Percent Recovery
		Method A (mg)	Method B (mg)	Reported method[9] (mg)	
Tablet I	100.00	99.98	99.99	99.98	100.50[a]
Tablet II	100.00	99.97	99.98	99.97	99.50[a]
Suspension	50.00	49.95	49.80	50.25	100.25[a]
Lactose	--	--	--	--	99.75[b]
Talc	--	--	--	--	101.00[b]
Magnesium Stearate	--	--	--	--	99.99[b]

* Average of six determinations.
a = Amount of nimesulidie added is 10 mg.
b = Amount of nimesulide added is 20 mg.

of upper Beer's law limits in each method were summarised in Table-1. When pharmaceutical preparations (Tablets and suspension) containing nimesulide were analysed the results obtained by the proposed methods (Table-2) are in good agreement with the labelled amounts and are comparable with the results of a reported method[9]. Recovery in both the methods is 99-101%. Method A is more sensitive than method B. Diluents and excipients present in the dosage forms did not interfere in the proposed methods.

The formation of colored species in method A is due to the diazotisation of reduced nimesulide followed by its coupling with pholoroglucinol to produce an azo dye[14]. The formation of 3:1 molar complex between reduced nimesulide and pholoroglucinol may be predicted as per the analogy by earlier workers[11,15,16]. In the case of method B, PDAB reacts with reduced nimesulide to form a colored schiff's base.

These results indicate that the proposed methods are sensitive, accurate, precise and reproducible and can be used for the routine determination of nimesulide in bulk and in dosage forms.

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