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Spectrophotometric Methods for Simultaneous Estimation of Nimesulide and Drotaverine

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ABSTRACT: Three simple spectrophotometric methods have been developed for simultaneous estimation of nimesulide and drotaverine from tablet dosage form. Method-I involves, formation of Q-absorbance equation at 349 nm (isoabsorptive point) and 298.5 nm (λ_{max} of nimesulide); Method-II simultaneous equation method involves the measurement of absorbances at two wavelengths 298.5 nm (λ_{max} of nimesulide) and 245 nm (λ_{max} of drotaverine) in ethanol (95%) and Method-III multicomponent mode of analysis involves the measurement of absorbances at two wavelengths 298.5 nm (λ_{max} of nimesulide) and 362.5 nm (λmax of drotaverine); The linearity lies between 5-30 µg/ml for both nimesulide and drotaverine for all the three methods. The accuracy and precision of the methods were determined and validated stastically. All the methods showed good reproducibility and recovery with % RSD less than 1. All method were found to be rapid, specific, precise and accurate and can be successfully applied for the routine analysis of nimesulide and drotaverine in bulk and combined dosage form.
Key Words: Nimesulide, drotaverine, Q-Absorbance ratio method, Multicomponent mode of analysis, Simultaneous equation method.

INTRODUCTION AND EXPERIMENTAL

Chemically, Nimesulide is 4- Nitro- 2- phenoxy-methanesulfonanilide[1]. It is a non-steroidal anti-inflammatory drug. It is used for chronic arthritis (such as rheumatoid arthritis and osteoarthritis); surgery and post-traumatic acute pain and inflammation; otorhinolaryngological inflammation resulting in pain; dysmenorrhea; upper respiratory tract infection symptoms such as fever treatment[2]. Nimesulide alone or in combination with other drugs is reported to be estimated by spectrophotometric method [3, 4], HPLC[5], TLC[6], HPTLC[7], GC[8] and capillary chromatographic method[9].

Chemically, Drotaverine is (1-(3, 4-diethoxybenzylidene)-6, 7-diethoxy-1, 2, 3, 4-tetrahydroisoquinoline) hydrochloride, is an isoquinoline derivative. It is a highly potent spasmolytic agent[10]. Drotaverine alone or in combination with other drugs is reported to be estimated by TLC densitometry[11]and differential spectrophotometric method[12].

Since no spectrophotometric method is reported for simultaneous estimation of nimesulide and drotaverine in combination therefore, in the present work, a successful attempt has been made to estimate both these drugs simultaneously by three simple UV-spectrophotometric methods (absorbance ratio method, Simultaneous equation method for analysis and Multicomponent mode method).

Instrument used is UV-Visible double beam spectrophotometer, Make: Shimadzu, Model No. 1700 with spectral bandwidth of 2 nm and a pair of 10 mm matched quartz cells. Pure drug samples of nimesulide and drotaverine were obtained as gift sample from Emcure Pharmaceuticals Ltd., Pune. Combined dose tablet formulation (NOBEL-SPAS) was procured from local medicine shop. Ethanol (95%) was used as solvent.

Preparation of stock solution: Accurately weighed quantity of nimesulide (5 mg) and drotaverine (5 mg) was transferred to two separate 50 mL volumetric flask, dissolved in 30 mL ethanol and diluted to the mark with the same solvent (stock solution:100 µg/mL).

Q-Absorbance ratio method (Method I): Q-Absorbance method uses the ratio of absorbances at two selected wavelengths, one at isoabsorptive point and other being the λ_{max} of one of the two compounds. From the stock solutions, working standard solutions of nimesulide (20 µg/mL) and drotaverine (20 µg/mL) were prepared by appropriate dilution and were scanned in the entire UV range to determine the maximum absorbance (λ_{max}) and isoabsorptive point. Nimesulide and

drotaverine have λ_{max} at 298.5 nm and at 245 nm, respectively. Both the drugs were found to have same absorbance at 349 nm (iso-absorptive point). The wavelengths selected for analysis were 349 nm and 298.5 nm respectively (Fig.1). A series of standard solutions ranging from 5-30 µg/mL for nimesulide and drotaverine both were prepared and the absorbance of solutions was recorded at 298.5 and 349 nm to plot a calibration curve of absorbance versus concentration. The calibration curves were found to be linear in the concentration range under study. Absorptivity values of nimesulide and drotaverine were determined at selected wavelengths and are presented in Table-1.

The concentration of two drugs in mixture was calculated by using following equations:

$$C_{NIME} = \frac{Q_m - Q_y}{Q_x - Q_y} \times \frac{A_1}{ax_1} \quad (1)$$

$$C_{DROTA} = \frac{Q_m - Q_x}{Q_y - Q_x} \times \frac{A_2}{ay_1} \quad (2)$$

Where A_1 and A_2 are the absorbances of mixture at 349 nm and 298.5 nm and ax_1 (13.9), ax_2 (20.3) and ay_1 (13.25), ay_2 (11.9) are absorptivities E (1%, 1 cm) of nimesulide and drotaverine at 349 nm and 298.5 nm and $Q_m = A_2/A_1$, $Q_y = ay_2/ay_1$ and $Q_x = ax_2/ax_1$.

Simultaneous equation method (Method – II): From the stock solution of 100 µg/mL, working standard solutions of drugs were prepared by appropriate dilution and were scanned in entire UV range to determine the λ_{max}. Nimesulide has λ_{max} of 298.5 nm while drotaverine has λ_{max} at 245 nm respectively (Fig.1). Standard solutions were prepared having concentration 5-30 µg/mL for both drugs. The absorbances of these standard solutions were measured at 298.5 nm and 245 nm and calibration curves were plotted at these wavelengths. Two simultaneous equations (in two variables C_1 and C_2) were formed using these Absorptivity coefficient values.

$$A_1 = (0.0203)\, C_1 + (0.0119)\, C_2 \quad (3)$$

$$A_2 = (0.0209)\, C_1 + (0.0258)\, C_2 \quad (4)$$

Where C_1 and C_2 are the concentrations of NIM and DRO measured in µg/mL, in sample solutions. A_1 and A_2 are the absorbances of mixture at selected wavelengths 298.5 nm and 245 nm respectively.

By applying the Cramer's rule to equation 1 and 2, the concentration C_{NIM} and C_{DRO}, can be obtained as follows,

$$C_{NIM} = \frac{A_2\,(0.0119) - A_1\,(0.0258)}{0.000275} \quad (5)$$

$$C_{DRO} = \frac{A_1\,(0.0209) - A_2\,(0.0203)}{0.000275} \quad (6)$$

Multicomponent mode of analysis (Method – III): 6 mixed standard solutions with concentration of nimesulide and drotaverine in the ratio of 20:20 µg/mL were prepared in ethanol (95%). All the standard solutions were scanned over the range of 400-200 nm, in the multicomponent mode, using two sampling wavelength 298.5 nm (λ_{max} of nimesulide) and 362.5 nm (λ_{max} of drotaverine). The data from these scans was used to determine the concentrations of two drugs in tablet sample solutions

Assay of tablet formulation by Method I, II & III: 20 tablets were weighed and crushed to obtain fine powder. An accurately weighed equivalent weight of tablet powder equivalent to about 100 mg of nimesulide and 40mg of drotaverine was transferred to 100 mL volumetric flask, dissolved in 20 mL ethanol (95%) and sonicated for 35 min. The volume was then made up to the mark using same solvent. The resulting solution was filtered through Whatmann filter paper grade I and filtrate was appropriately diluted to get approximate concentration of 20 µg/mL of nimesulide and 8 µg/mL of drotaverine.12µg/mL of drotaverine was added externally to obtain the concentration of 20µg/mL of both the drugs in final sample solutions. Absorbances of sample solutions were recorded at 298.5 nm and 349 nm and the concentration of two drugs in the sample were determined by using eqns. 1 and 2 (Method-I).

The tablet sample solution was also subjected to analysis by simultaneous equation method. Absorbances of sample solutions were recorded at 298.5 nm (λ_{max} of nimesulide) and 245 nm (λ_{max} of drotaverine) and concentration of two drugs in the sample were determined by using equations 5 and 6.

The same tablet sample solutions were subjected to analysis in the multicomponent mode of instrument. The solution was scanned over the wavelength range of 400-200 nm. 298.5 nm was used as λ_{max} of nimesulide and 362.5 nm as λ_{max} of drotaverine the concentration of each drug was determined by analysis of spectral data of the sample solution with reference to the mixed standards.

The analysis procedure was repeated 6 times with tablet formulations. The result of analysis of tablet formulation is reported in Table- 2.

Recovery studies: To study the accuracy of the proposed methods, recovery studies were carried out by standard addition method at three different levels. A known amount of drug was added to preanalyzed tablet powder and percentage recoveries were calculated. The results of recovery studies were satisfactory and are presented in Table-3.

RESULTS AND DISCUSSION

For all the three methods linearity was observed in the concentration range of 5-30 µg/ml for both nimesulide and drotaverine. Marketed brand of tablet was analyzed and amount of drug determined by proposed methods ranges from 99.83 to 100.12 as shown in Table-

2. The proposed methods were validated as per ICH guideline. The accuracy of method was determined by calculating mean percentage recovery. It was determined at 80,100 and 120 % level. The % recovery ranges from 99.60 to 100.29 for all the three methods and are presented in Table 3.Precision was calculated as repeatability (% RSD is less than 1) and inter and intraday variations (%RSD is less than 1) for both drugs. The repeatability data, ruggedness data are presented in Table-3.

The proposed methods were found to be simple, accurate and rapid for the routine determination of nimesulide and drotaverine in tablet formulation. To study the validity and reproducibility of proposed methods, recovery studies were carried out. The methods were validated in terms of linearity, accuracy, precision, specificity and reproducibility. The three methods can be successfully used for simultaneous estimation of nimesulide and drotaverine in combined dosage form.

Table – 1: Absorptivity values (E 1%, 1 cm) of nimesulide (NIM) and drotaverine (DRO) at 349 nm (isoabsorptive point) and 298.5 nm (Method -I)

S. NO.	Absorptivity at 349 nm		Absorptivity at 298.5 nm	
	NIM	DRO	NIM	DRO
1.	13.87	13.28	20.33	11.87
2.	13.90	13.27	20.30	11.92
3.	13.93	13.25	20.34	11.90
4.	13.95	13.22	20.27	11.88
5.	13.90	13.25	20.30	11.93
6.	13.85	13.23	20.26	11.90
Mean	13.90	13.25	20.30	11.90
S. D.	±0.0369	±0.0228	±0.0316	± 0.0228
RSD (%)	0.26546	0.17207	0.15566	0.19159

Table-2: Results of simultaneous estimation of marketed formulation (Nobel-Spas, Mankind) for Method I, II & III

Method	Tablet content	Label claim (mg/tab)	Label claim* (%)	±SD*	RSD (%)*
I	NIM	100.0	100.12	±0.2164	0.21614
	DRO	40.0	99.86	±0.3133	0.31373
II	NIM	100.0	100.020	±0.1557	0.15564
	DRO	40.0	99.991	±0.1897	0.18975
III	NIM	100.0	99.825	±0.4845	0.48535
	DRO	40.0	100 .025	±0.4228	0.42267

***Mean of six estimations; NIM = Nimesulide; DRO = Drotaverine**

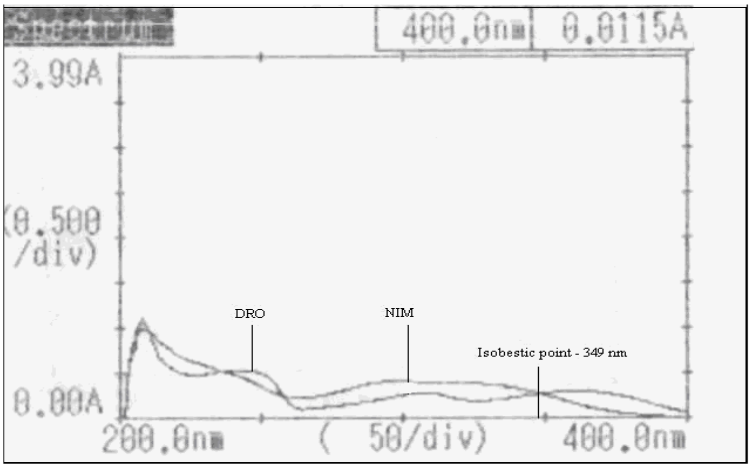

Fig. 1: Overlain spectra of Nimesulide (NIM) and Drotaverine (DRO)

Table-3: Results for recovery studies

Level of recovery	Amt of drug added µg/ml	Drug	Method I		Method II		Method III	
			Recovery (%)*	±SD*	Recovery (%)*	±SD*	Recovery (%)*	±SD*
80%	16	NIM	100.20	±0.065	100.02	±0.038	99.95	±0.376
	16	DRO	99.74	±0.102	100.15	±0.112	99.82	±0.188
100%	20	NIM	100.28	±0.020	99.91	±0.072	100.28	±0.176
	20	DRO	99.60	±0.055	100.29	±0.047	99.88	±0.262
120%	24	NIM	100.23	±0.081	99.97	±0.075	99.99	±0.134
	24	DRO	99.72	±0.125	100.02	±0.272	99.96	±0.284

***Mean of six estimations; NIM =Nimesulide; DRO =Drotaverine**

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