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Determination of drotaverine and nimesulide in combined tablet dosage form by ratio derivative spectroscopy and dual wavelength spectrophotometric methods

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ABSTRACT

Two simple, economical, precise and accurate methods for simultaneous determination of Drotaverine (DRT) and Nimesulide (NIM) in combined dosage form have been developed. The first method is Ratio Derivative spectroscopy method (Method A) in which ratio derivative amplitudes were measured at selected wavelengths. Second method is Dual wavelength Spectrophotometry (Method B). The amplitudes at 344.8 nm and 243.5 nm in the Ratio derivative spectra were selected to determine DRT and NIM, respectively and wavelengths 254.008, 274.68 nm and 221.09, 232.067 nm were selected to determine DRT and NIM, respectively by dual wavelength method in methanol. Beer's law is obeyed in the concentration ranges of 8-24 µg mL^{-1} and 20-60 µg mL^{-1} for DRT and NIM, respectively in methanol for both the methods. The % assay for commercial formulation was found to be in the range 99.91–100.91% for DRT and 99.84 – 101.07% for NIM by the proposed methods. Recovery was found in the range 99.18-100.10 for DRT and 99.52 – 101.09% for NIM by ratio derivative spectroscopic method and 99.82 – 101.12% for DRT and 99.73-101.09% for NIM by dual wavelength method for both the Formulations. The results of analysis have been validated statistically and recovery studies confirmed the accuracy and of the proposed methods which were carried out by following ICH guidelines.

Keywords: Drotaverine, Nimesulide, Ratio Derivative Spectroscopy, Dual wavelength.

INTRODUCTION

Drotaverine hydrochloride [DRT], 1-[(3, 4-diethoxy phenyl) methylene]-6, 7-diethoxy-1, 2, 3, 4-tetra hydro isoquinolene is an analogue of papaverine [1]. It acts as an antispasmodic agent by inhibiting phosphodiesterase IV enzyme, specific for smooth muscle spasm and pain, used to reduce excessive labor pain [2]. Drotaverine hydrochloride is official in Polish Pharmacopoeia. A few UV spectrophotometric [3-6, 20] and HPLC [7-9,18-19] methods have been reported individually or in combination with other drugs for estimation of Drotaverine hydrochloride.

Nimesulide [NIM] is chemically designated as 4-nitro-2-phenoxymethane sulfonilide ($C_{13}H_{12}N_2O_3S$) [10, 11]. It is a new non-steroidal anti-inflammatory drug (NSAIDS) with analgesic antipyretic properties that does not induce gastrointestinal ulceration. It is an inhibitor of prostaglandin synthesis from arachidonic acid and of platelet aggregation. Various UV, HPLC and stability indicating LC methods for NIM have been reported for its estimation individually or in combination with other drugs [12-16]. As per our knowledge Absorbance ratio method, Simultaneous equation method, and First order derivative method are available in the literature for the simultaneous estimation of DRT and NIM in combined dosage form [17-20]. Present manuscript describes Ratio Derivative and dual wavelength spectroscopic methods for the determination of DRT and NIM in tablet dosage form. The proposed methods were validated as per the International Conference on Harmonization (ICH) guidelines [21].

MATERIALS AND METHODS

Instrumentation

An UV-Visible double beam spectrophotometer (Varian Cary 100) with 10 mm matched quartz cells was used. All weighing were done on electronic balance (Model Shimadzu AUW-220D), High Speed Centrifuge Research Centrifuge (Biolab, BL-165D), Ultrasonicator model 5.5L150H were used.

Reagents and chemicals

Spectroscopic grade Methanol was purchased from LOBA Chemie Pvt. Ltd., Mumbai. Tablet used for analysis were NOBEL SPAS (Batch No. NBS 002 & 003) marketed by Mankind Pharma Ltd, Okhala Industrial Estate-3,New Delhi, India containing DRT 40 mg and NIM 100 mg per tablet. Pharmaceutical grade of Droaverine (% purity, 99.78) was kindly supplied as a gift sample by Alkem Pharmaceuticals, Mumbai, India and pure drug sample of NIM (% purity, 99.92) was gifted by New Life Pharmaceuticals, Pune, India. These samples were used without further purification.

Preparation of Standard Stock Solutions and calibration Curve

Standard stock solution of pure drug containing 1000 µg mL^{-1} of DRT and 1000 µg mL^{-1} of NIM were prepared separately in the methanol. The working standard solutions of these drugs were obtained by dilution of the respective stock solution in methanol. The Ratio Derivative amplitudes of spectrum, by using the above mentioned procedures, were used to prepare calibration curves for both the drugs. For verification of Beer's law a series of dilutions in the concentration range of 8-24 µg mL^{-1} for DRT (series A) and 20-60 µg mL^{-1} for NIM(series B) were prepared for both the methods and mixture of both the drugs (series C) in same concentration range was prepared.

Method A:

Ratio Derivative Method:

The method involves dividing the spectrum of mixture by the standardized spectra of each of the analyte and deriving the ratio to obtain spectrum that is dependent of concentration of analyte used as a divisor. Using appropriate dilutions of standard stock solution, the two solutions were scanned separately. The ratio spectra of different DRT standards at increasing concentrations were obtained by dividing each with the stored spectrum of the standard solution of NIM (40 µg mL^{-1}) and the first derivative of these spectra traced, illustrated in Fig 1. Wavelength 344.8 nm was selected for the quantification of DRT in DRT+NIM mixture. The ratio and ratio derivative spectra of the solutions of NIM at different concentrations were obtained by dividing each with the stored standard spectrum of the DRT (16

μg mL^{-1}) [Fig. 2]. Wavelength 243.5 nm was selected for the quantification of NIM in DRT+ NIM mixture. Measured analytical signals at these wavelengths were proportional to the concentrations of the drugs. Calibration curves were prepared from the measured signals at the selected wavelength and concentration of the standard solutions. The amount of DRT (C_{DRT}) and NIM (C_{NIM}) in tablets was calculated by using equations 1 and 2, respectively.

C_{DRT} = [Derivative amplitude at 344.8 – (0.0006)] / (0.0806) ... (1)
C_{NIM}= [Derivative amplitude at 243.5 – (0.0429)] / (1.2221) .... (2)

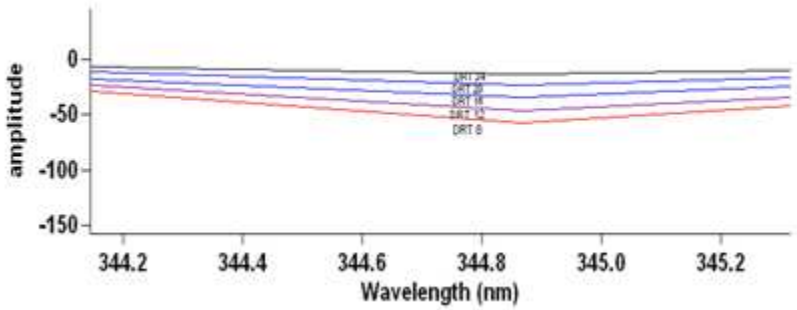

Fig 1. First derivative of the ratio spectra of DRT solution (8– 24 μg mL^{-1}) when 40μg mL^{-1} solution of NIM is used as divisor.

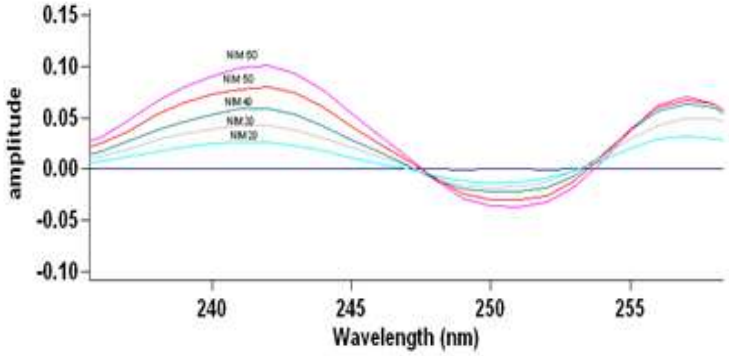

Fig2. First derivative of the ratio spectra of NIM solution (20-60 μg mL^{-1}) when 16 μg mL^{-1} solution of DRT is used as divisor

Method B:

Dual Wavelength Method:

The spectrum of DRT shows identical absorbance at 254.008 nm (λ_3) and 274.68 nm (λ_4) therefore these two wavelengths were selected for the analysis of NIM. All the solutions of **series A** were scanned to ensure that the difference between λ_3 and λ_4 is zero. Similarly, the NIM solutions were scanned to determine the two wavelengths, where absorbance is same. These two wavelengths were found to be 221.09 nm (λ_1) and 232.067 nm (λ_2). All the solution of **series B** were scanned to ensure that difference between (λ_1) and (λ_2) is zero. Thereafter, the solution of **series C** were scanned to ensure that varying concentration of NIM and DRT are not affecting the absorbance at selected wavelength. The method was used to analyse marketed preparation.

Formulation Analysis:

A quantity of powder from twenty tablets equivalent to 40 mg of DRT (100 mg of NIM) was weighed and transferred to 50 ml flask containing of methanol, and ultrasonicated for 10 min and centrifuged for 10 min at 10000 RPM. Supernatant was transferred to 25 ml volumetric flask and volume was made up to mark. The solution was filtered and suitably diluted with methanol to

have 16 µg mL^{-1} of DRT and 60µg mL^{-1} of NIM. The proposed methods were then followed to determine concentration of analytes in the sample solutions.

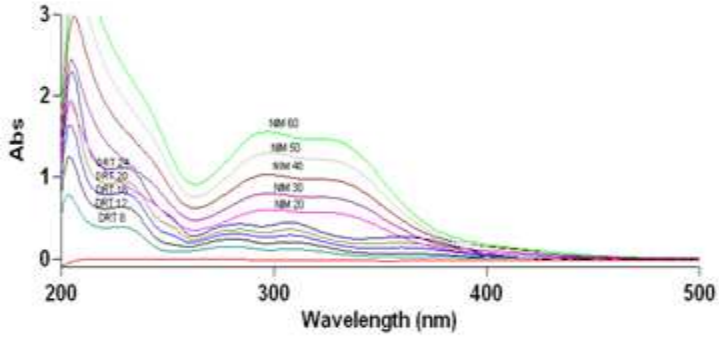

Fig 3. Overlain spectra of Drotaverine (8–24µg mL^{-1}) and Nimesulide(20-60µg mL^{-1}) in methanol.

Table 1: Optical characteristics of the proposed methods and Results of precision and formulation analysis

Parameter		Drotavarine		Nimesulide	
		Method A	Method B	Method A	Method B
λ (nm)		344.8 nm	Difference in absorbance between 254.008-274.68 nm	243.5 nm	Difference in absorbance between 221.09-232.067 nm
Beer's law range (µg mL^{-1})		8-24	8-24	20-60	20-60
Regression Equation (y = mx + c)	Slope (m)	0.0806	0.00104	1.2221	0.00279
	Intercept (c)	0.0006	0.03134	0.0429	0.02063
Correlation coefficient		0.999	0.999	0.999	0.999
Precision %R.S.D.	Repeatability (n=6)	0.52	0.97	1.12	0.98
	Intra-day (3×5 imes)	0.64	1.02	1.02	0.87
	Inter-day(3×5 days)	0.51	0.91	0.97	0.75
	Analyst	0.69	0.88	0.89	0.80
Tablet Analysis (%Assay, %RSD) n=6	Tablet I	99.91, 0.89	100.91, 0.85	99.84,1.02	101.07, 0.62
	Tablet II	100.01, 0.92	99.78, 1.21	100.10,0.92	99.07, 0.83

Recovery Method

The accuracy of the proposed methods was checked by recovery study, by addition of standard drug solution to preanalysed sample solution at three different concentration levels (50 %, 100 % and 150 %) within the range of linearity for both the drugs. The basic concentration level of sample solution selected for spiking of the drugs standard solution was 16 µg mL^{-1} of DRT and 60 µg mL^{-1} of NIM for both the methods.

Table 2: Results of Recovery studies of DRT and NIM by the proposed methods

Formulation studies	Recovery Level	Recovery of	% Mean Recovery, % RSD by	
			Method A	Method B
Tablet I, n = 3	50%	DRT	101.25,0.57	100.12,0.42
		NIM	99.50,0.78	100.52,0.83
	100%	DRT	99.98,0.69	100.58,1.07
		NIM	100.09,1.24	99.87,0.97
	150%	DRT	100.95,0.96	101.32,0.84
		NIM	101.75,0.69	101.23, 1.09
Tablet II, n = 3	50%	DRT	99.85,0.79	100.35,0.77
		NIM	101.22,0.58	100.25,1.24
	100%	DRT	100.98,0.55	102.12,1.27
		NIM	100.09,0.79	101.39,0.68
	150%	DRT	100.09,0.29	99.99,0.89
		NIM	102.45,0.76	101.65, 0.48

Precision of method:
Repeatability of the methods were determined by repeating the procedure six times. To study intraday precision, methods were repeated 5 times in a day and the average % RSD was calculated. Similarly the methods were repeated on five different days and average % RSD was calculated. Method was repeated by another analyst working in the same laboratory to know the precision of analyst. The values confirm the intra and inter day precision.

RESULTS AND DISCUSSION

The proposed methods for simultaneous estimation of DRT and NIM in combined dosage form were found to be accurate, simple and rapid. The developed methods can be used for routine analysis of two drugs in combined dosage forms. Practically no interference from tablet excipients was observed in these methods. Both the methods are accurate, simple, rapid, precise, reliable, sensitive, reproducible and economic [Table 1]. The values of % RSD for both the method first order ratio derivative spectra (Tablet) were found to be < 2 (% RSD 0.51-1.12 and 0.75-1.02). The result of recovery studies for Tablet was found to be 99.95-101.45 for method A and 99.99-102.12 for method B [Table 2], for DRT , and 99.50-102.45 for method A 99.87-101.65 for method B indicates that there is no interference due to excipients present in the formulation. It can be easily and conveniently adopted for routine quality control analysis.

CONCLUSION

The proposed methods are simple, precise, accurate, economical and rapid for the determination of DRT and NIM in combined tablet dosage forms. Analysis of authentic samples containing DRT and NIM showed no interference from the common additives and excipients. Hence, recommended procedure is well suited for the assay and evaluation of drugs in pharmaceutical preparations. It can be easily and conveniently adopted for routine quality control analysis.

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REFERENCES

[1] The Merck Index – An Encyclopedia of chemicals, Drugs, and biological, Merck Research Laboratories, Whitehouse station, New Jersey: **2001**, 13, 6, 609-10.
[2]S. Sethi, Textbook of Pharmacology. Elsevier, New Delhi: **2004**, 831-40.
[3] P. Dahivelkar, S. Bari, *Indian J. Pharm. Sci*., **2007**, 69, 812-814.
[4] P. Dahivelkar, S. Surana, *Indian Drug*s, **2006**, 43, 896-900.
[5]F. Metwally , M. Abdelkawy, *J. AOAC Int*., **2006**, 89, 78-81.
[6]H. Abdellatif, M. Ayad, *Chem. Pharm. Bull*., **2006**, 54, 807-13.
[7]D. Panigrahi, R. Sharma, *Acta Chromatographica*, **2008**, 20, 439–50.
[8]J. Mezei, S. Kuttel, *J. Pharm. Sci*., **1984**, 73, 1489-91.
[9]P. Dahivelkar, S. Bari, S. Bhoir, A. Bhagwat, *Iranian J. Pharm. Research*, **2009**, 8, 209-15.
[10] Martindale - The Complete Drug Reference, RPS Publishing, Great Britain, 36, **2009**, 14-5.
[11] Indian Pharmacopoeia, Indian Pharmacopoeia Commission, Ghaziabad: **2007**, 2, 63-4.
[12] A. Nikam, S. Sampada, S. Gandhi, *I. J..Pharm.Sci*., **2008**, 70, 635-7.
[13] R. Shah, S. Magdum Patil, D. Chougule, N. Naikwade, *Research J. Pharm. and Tech*., **2008**, 1, 430-2.

[14] P. Musmade, G. Subramanian, K. Srinivasan, *Analytica Chimica Acta*, **2007**, 585, 103–109.
[15]M. Momin, P. Yeole, M. Puranik, S. Wadher, *Indian J. Pharm. Sci*., **2006**, 68, 387-9.
[16] N. Hasan, E. Abdel, B. Elzeany, N. Wagieh, *Il Farmaco*, **2003**, 58, 91-9.
[17] V. Rajmane, S. Gandhi, U. Patil, M. Sengar, *Eurasian J. Anal. Chem*, **2009**, 4, 184- 90.
[18] Suganthi Azhlwar et al *Der Pharmacia Lettre*, **2010**, 2(2): 328-332
[19] Kabeer A. Shaikh et al *Der Pharmacia Lettre*, **2010**, 2(4): 355-364
[20] Khaggeswar. B et al *Der Pharmacia Lettre*, **2011**, 3(1):166-176