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SPECTROPHOTOMETRIC METHOD FOR THE SIMULTANEOUS ESTIMATION OF PARACETAMOL AND DOMPERIDONE IN TABLET DOSAGE FORMS

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ABSTRACT

A simple, precise and economical procedure have been developed for the simultaneous estimation of Domperidone (DOM) and Paracetamol (PML) involves absorbance measurement at 284.5nm and 244.2nm corresponding to the respective absorption maxima. Both the drugs obey Beer's law in the range of 0.1-80µg/ml for Domperidone and 1-50µg/ml for Paracetamol. The tablet formulations were evaluated for the percent content of both the drugs at the selected wavelengths. The result of analysis has been validated statistically by repeatability and recovery studies. The results were found satisfactory and reproducible. The method was applied successfully for the estimation of DOM and PML simultaneously in tablet dosage form without the interference of common excipients.

Key Words: Domperidone, Paracetamol, Beer's law, Repeatability, Recovery studies

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INTRODUCTION

Domperidone is an antiemetic and antinauseant and acts on dopamine receptor system as an antagonist. Chemically it is 5-chloro-1-[1-(2,3-dihydro-2-oxo-1H-benzimidazole-1-yl) propyl)-4-piperidyl]-2,3-dihydro-1H-benzimidazol-2-one. Paracetamol, chemically 4-hydroxy acetanilide, is a centrally and peripherally acting non-opioid analgesic and antipyretic. A combination of these drugs is available as tablets for clinical practice. Their combination is used for the treatment of migraine. A survey of literature reveals that various methods like HPLC [1-4], NMR, U.V [5-13] are available for individual determination of Domperidone and Paracetamol. However there is no spectrophotometric method for the simultaneous determination of the Domperidone and Paracetamol. An attempt was made to develop accurate, precise, reproducible and economical method for the simultaneous estimation of both these drugs in combined dosage form.

MATERIALS AND METHODS

Material

The pure sample of DOM was procure from Tri-Star pharmaceuticals, Pondicherry and PML was procured from Medopharm pharmaceuticals, Chennai. The authenticity and purity of the samples were certified by the same.

Domcet (Protec) and Grenil (Karnataka antibiotics and Pharmaceuticals Ltd.) were procured from local pharmacy. Domcet contains DOM-10mg and PML-500mg, whereas Grenil contains DOM-20mg and PML-500mg.

Instrument

A Shimadzu 1601 UV Spectrophotometer with 1cm matched quartz cells and single pan electronic balance-Digitek was used for the estimation.

Chemicals and Reagents

1N glacial acetic acid AR grade and distilled water was used during the experiment.

Preparation of standard stock solution

The standard stock solution of both DOM and PML were prepared separately by dissolving 100mg each of DOM and PML in 100ml volumetric flask separately using 1N glacial acetic acid as a solvent to give a concentration of 1000µg/ml.

Absorption maximum (λ_{max})

The stock solution were suitably diluted with 1N glacial acetic acid so as to contain 5µg/ml of DOM and 9µg/ml of PML respectively. The solutions were scanned in the UV region between

400-200nm and found that DOM exhibited λ_{max} at 284.5nm and PML exhibited λ_{max} at 244.2nm.

Beer's law concentration range

The stock solutions were suitably diluted with 1N glacial acetic acid to get concentration range from 0.1-1000µg/ml for DOM and 1-1000µg/ml for PML. The solutions were scanned in the UV region between 400-200nm and their absorbance's were measured at respective maxima (λ_{max}) points. Using the absorbance values against concentrations plotted the calibration curve. From the graphs it was found DOM and PML obeys Beer's law between 0.1-80µg/ml and 1-50µg/ml respectively. The regression analysis was carried out for the regression line which estimates the degree of linearity.

Stability of absorbance

The stability of the solutions was checked by measuring the absorbance at regular intervals of time. It was observed that the absorbance remained stable for a period of more than 120 minutes which is sufficient for proposed work.

Preparation of mixed standard stock solution

Dom 20mg and PML 500mg were accurately weighed and dissolved in 1N glacial acetic acid to get concentration of 0.32µg/ml, 8µg/ml of DOM and PML respectively. The solution of DOM and PML was scanned in the wavelength range of 400-200nm.

Estimation of drug from tablet dosage form sample solution

Twenty tablets were finely powdered. An accurately weighed quantity of powder equivalent to about 100mg of paracetamol was transferred to a 100ml volumetric flask. The content of the flask was mixed with 1N glacial acetic acid and shaken to dissolve the active ingredients and then made up to the volume with the same solvent. The solution was filtered and the filtrate was further diluted with 1N glacial acetic acid to give a final drug concentration of 0.1-2.0µg/ml and 5-50µg/ml of DOM and PML respectively. Absorbance values of sample solution was recorded at 284.5nm as A_2 and 244.2nm as A_1.

Repeatability

Repeatability expresses the precision under the same operating conditions. It is also termed as intra-assay precision. It is assessed by using a minimum of nine determinations for each tablet dosage form covering the specified range for the procedures. (three concentrations/three replicates each).

Recovery studies

The recovery studies were carried out at the different concentrations by spiking a known concentration of standard drug to the pre analyzed sample and contents were analyzed by proposed methods.

RESULTS AND DISCUSSION

The UV spectra of DOM and PML are presented in Fig-1 and 2 respectively. The absorption maxima (λ_{max}) were observed at 284.5nm and 244.2nm for Domperidone and Paracetamol respectively. Obeyance to Beer's law was confirmed by the linearity of the calibration curve of Dom and PML, which are represented in Fig-3 and 4.

DOM shows the linearity in the concentration range of 0.1-80µg/ml and PML showed linearity in the concentration range of 1-50µg/ml. The overlain spactra for the linearity of DOM and PML are represented in Fig-5 and 6. Absorptivity values for DOM and PML were calculated and are presented in Table 1 and 2.

The quantitative estimation was carried out on two different brands of tablet formulations by taking a concentration of 0.14 and 0.28µg/ml for DOM and 7µg/ml of PML. The data regarding the quantitative estimation is given in Table-3. The overlain spectra of standard DOM and PML and mixed standards are given in Fig-7 and 8. Both the brands of formulations show percentage purity values ranging from 98.40% to 101.53%w/w for DOM and 98.0% to 102.78%w/w of PML. The percentage deviation values were found to lie between -1.60 to +1.53 for DOM and -2.0 to 2.78 for PML.

The quantitative results obtained were subjected to statistical analysis to find out standard deviation and standard error values. The relative standard deviation values are below 2%, indicating the precision of methodology and low standard error values show the accuracy of the method. The statistical data is given in Table-4.

The validation of the proposed simultaneous equation method was further confirmed by repeatability and recovery studies. By repeating the assay procedure with three different concentrations of three replicates each, the repeatability of the method was confirmed. The data is given in Table-5. The result obtained in repeatability test expresses the precision of the proposed method.

The recovery data is given in Table-6. The percentage recovery values vary from 98.75% to 99.75% for DOM and 98.13% to 100% for PML. This serves as a good index of accuracy and reproducibility of the study.

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Table: 1: ABSORPTIVITY VALUES OF DOMPERIDONE AND PARACETAMOL
SAMPLE 1

Concentration (µg/ml)		Absorptivity at 244.2nm		Absorptivity at 284.5nm	
		ax_1	ay_1	ax_2	ay_2
PARA	DOMP	PARA	DOMP	PARA	DOMP
5	0.10	625.00	190.00	92.60	490.00
6	0.12	605.83	200.00	91.50	491.67
7	0.14	654.00	192.86	98.00	485.71
8	0.16	648.62	206.25	94.12	487.50
9	0.18	647.66	211.11	95.77	461.11

Table: 2: ABSORPTIVITY VALUES OF DOMPERIDONE AND PARACETAMOL
SAMPLE 2

Concentration (µg/ml)		**Absorptivity at 244.2nm**		**Absorptivity at 284.5nm**	
		ax_1	**ay_1**		**ax_1**
PARA	DOMP	PARA	PARA	DOMP	PARA
5	0.20	625.00	5	0.20	625.00
6	0.24	605.83	6	0.24	605.83
7	0.28	654.00	7	0.28	654.00
8	0.32	648.62	8	0.32	648.62
9	0.36	647.66	9	0.36	647.66

Table: 3: QUANTITATIVE ESTIMATION OF DOMPERIDONE AND PARACETAMOL

Tablet sample	**Drug**	**Label claim (mg/Tab)**	***Amount present (mg/tab)**	**Percentage Label claim (% w/w)**	**Percentage Deviation**
Sample-A	PARA	500	497.42	99.48	-0.52
	DOMP	10	10.03	100.27	+0.27
Sample- B	PARA	500	500.76	100.15	+0.15
	DOMP	20	19.94	99.72	-0.28

***Each value is the mean of five readings.**

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Table-4: STATISTICAL DATA

Tablet Sample	Drug	Percentage label claim	Standard Deviation (S.D)	Relative Standard Deviation (R.S.D)	Standard Error of Mean (S.E)
Sample-A	DOM	100.27	0.6407	0.0064	0.2865
	PML	99.48	1.3293	0.0134	0.5945
Sample-B	DOM	99.72	1.2873	0.0129	0.5757
	PML	100.15	2.2026	0.0219	0.9851

***Each value is the mean of five readings.**

Table-5: REPEATABILITY

Tablet Sample	Concentration (µg/ml)		Label claim (mg/tab)		Amount Found (mg)		Percentage label claim (%w/w)		Percentage deviation	
	DOM	PML	DOM	PML	DOM	PML	DOM	PML	DOM	PML
Sample-A	0.12	6	10	500	10.06	502.03	100.58	100.41	+0.58	+0.41
	0.14	7			10.08	502.42	100.83	100.48	+0.83	+0.48
	0.16	8			10.03	492.25	100.27	98.45	+0.27	-1.55
Sample-B	0.24	6	20	500	19.84	494.60	99.20	98.92	-0.80	-1.08
	0.28	7			20.31	494.29	101.55	98.86	+1.55	-1.14
	0.32	8			19.94	513.13	99.70	102.63	-0.30	+2.63

Each value is the mean of three readings.

Table-6: RECOVERY STUDIES

Tablet Sample	Drug	Lable claim (mg/tab)	Concentration (µg/ml)	Amount of standard added (mg)	Amount estimated (mg)	Percentage recovery (%w/w)	Percentage deviation
Sample-A	DOM	10	0.12	100	109.17	99.17	-0.83
			0.14		109.71	99.71	-0.29
			0.16		109.75	99.75	-0.25
	PML	500	6	100	598.33	98.33	-1.67
			7		598.57	98.57	-1.43
			8		600.00	100	0.00
Sample-B	DOM	20	0.24	100	119.17	99.17	-0.83
			0.28		119.14	99.14	-0.86
			0.32		118.75	98.75	-1.25
	PML	500	6	100	598.33	98.33	-1.67
			7		598.57	98.57	-1.43
			8		598.13	98.13	-1.87

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Fig-1: SPECTRUM OF DOMPERIDONE STANDARD

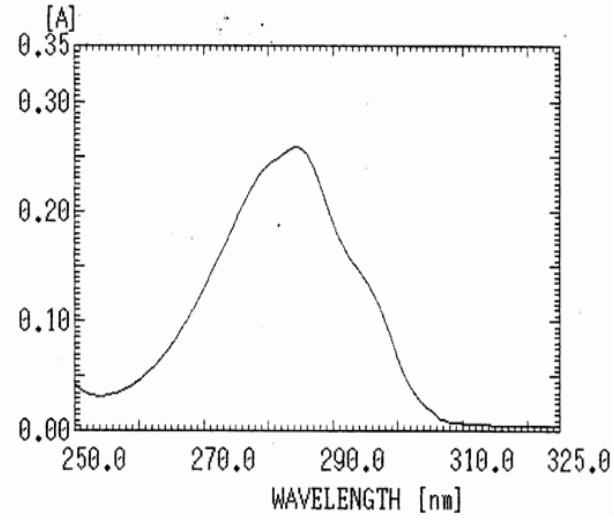

Fig-2: SPECTRUM OF PARACETAMOL STANDARD

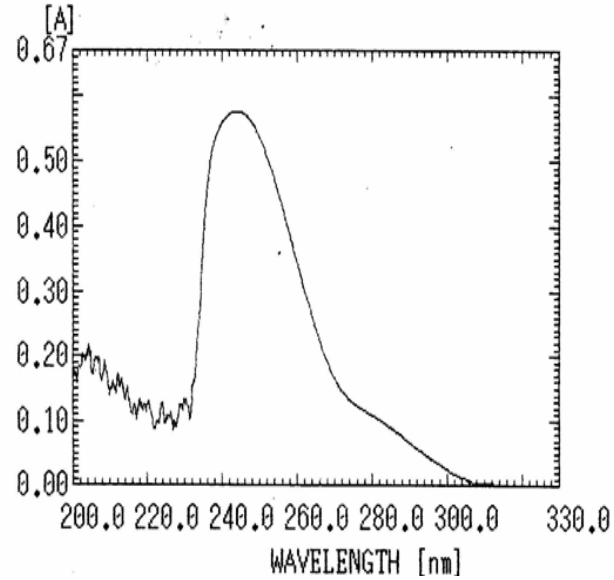

Fig-3:

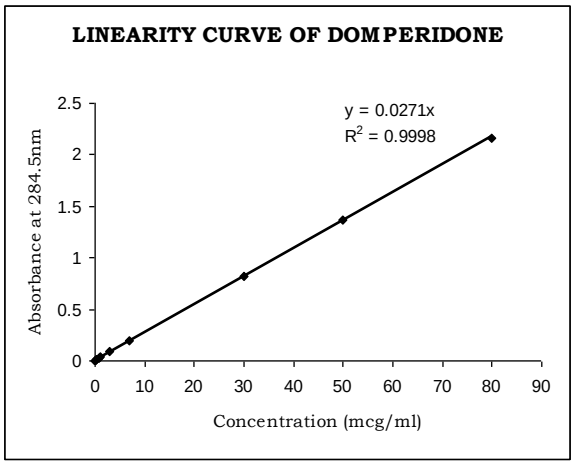

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Fig-4

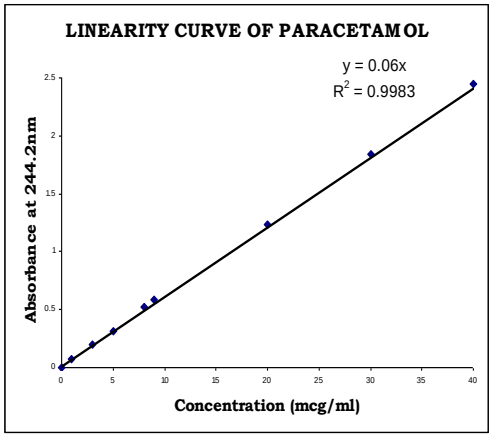

Fig- 5

OVERLAY SPECTRUM OF DOMPERIDONE STANDARD

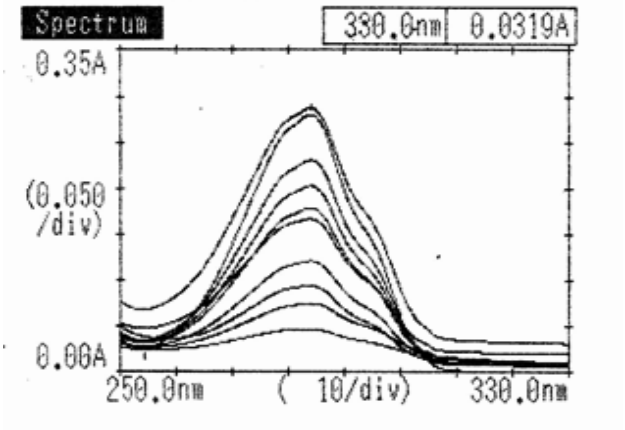

Fig-6: OVERLAY SPECTRUM OF PARACETAMOL STANDARD

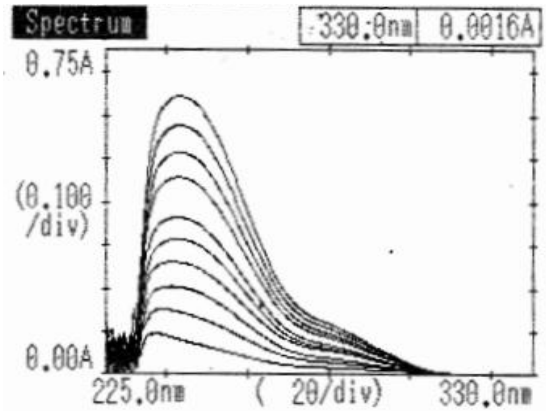

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Fig-7: OVERLAY SPECTRUM OF DOMPERIDONE AND PARACETAMOL STANDARD

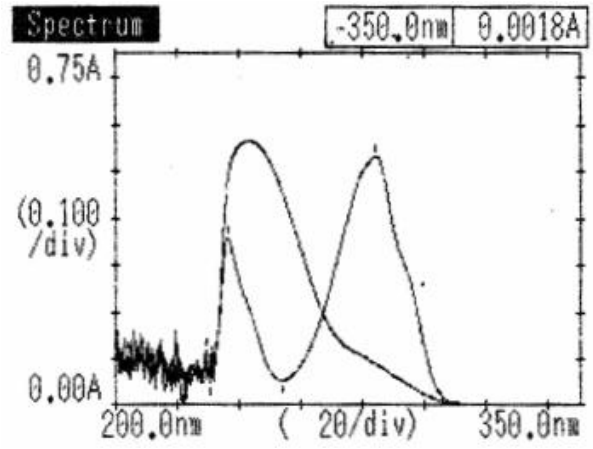
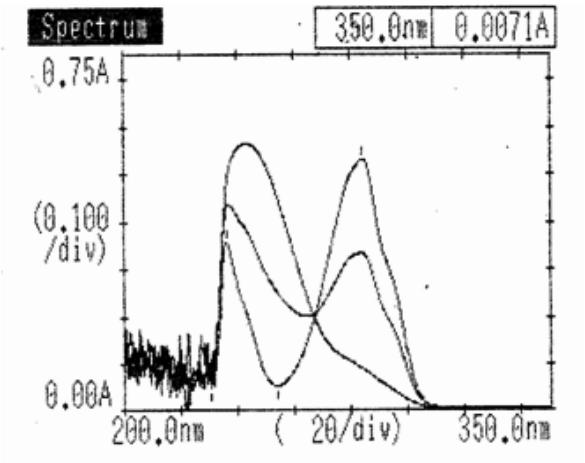


Fig-8: OVERLAY SPECTRUM OF DOMPERIDONE, PARACETAMOL AND MIXED STANDARDS



CONCLUSION

Analytical method plays a vital role in new drug development, preformulation and formulation studies, stability studies, quality control testing and in quality assurance programmes. So analysis are always in search of developing rapid and accurate new method of analysis that are able to exist in routine analytical work. The present analytical work comprises of simple, precise, rapid, sensitive and accurate method for the simultaneous estimation of Domperidone and Paracetamol in combined tablet dosage forms without any interference from the excipients.

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