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Simultaneous UV Spectrophotometric estimtion of Metoclopramide hydrochloride and Paracetamol in solid dosage form

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Abstract:
A simple, specific, accurate, precise and reproducible method has been developed and validated for the simultaneous estimation of metoclopramide hydrochloride and paracetamol in combined dosage form by UV Spectrophotometric method. UV Spectrophotometric method includes Simultaneous Equation method (Method I), Absorbance Ratio method (Method II) and correction method (Method III), For development of Method I, wavelengths selected were 243.0 nm and 273.5 nm for estimation of metoclopramide hydrochloride (MET) and paracetamol (PAR) respectively while for Method II, 243.0 nm λ_{max} for paracetamol, 262.0 nm Isoabsorptive point of Par and Met and 309.0 nm for correction method. The two drugs follow Beer-Lambert's law over the concentration range of 4-16 µg/mL for MET and 4-16 µg/mL for PAR. The % estimation of the drugs was found near to 100 % representing the accuracy of the three methods. The recovery of the MET and PAR were found near to 100 %. Validation of the proposed methods was carried out for its accuracy, precision, specificity and ruggedness according to ICH guidelines. The proposed methods can be successfully applied in routine work for the determination of metoclopramide hydrochloride and paracetamol in combined dosage form.
Keywords: Metoclopramide hydrochloride, Paracetamol, UV spectroscopy, Simultaneous Equation method, Absorbance Ratio method, Absorbance Correction method.

Introduction:

Paracetamol (PAR) is chemically N-(4-hydroxyphenyl) acetamide. It is used mainly as antipyretic[1]. Metoclopramide (MET) is 4-amino-5-chloro N-(2-diethyalaminoethyal)-2-methoxy benzamide. It finds its use as antiemetic[2]. Literature survey reveals that gas chromatography[4] HPLC[5], titrimetric[6] and densitometric methods[7] are available for the determination of paracetamol and spectrophotpmetric[8] HPLC[9] and H NMR[10] spectroscopic method for the determination of Metoclolpramide. The review of literature revealed that no method is yet reported in solvent milli-Q water for the simultaneous determination of both the drugs in combined dosage form. This paper describes three simple, rapid, accurate, reproducible and economical methods for the simultaneous determination of metoclopramide and paracetamol from tablet formulation.

Materials and methods:

Instrument

SHIMADZU double beam UV-visible spectrophotometer (model 1700) with 1 cm matched quartz cuvettes were used for all absorbance measurements. Shimadzu AUX220 balance was used for weighing the samples**.** All the chemicals used were of AR grade. Milli-Q water and Whatmann filter paper (no.41) were used throughout the experimental work.

Materials

Multicomponent tablet METOPAR (MET 5mg and PAR 500.mg) manufactured by cosme farma laboratories limited, karnataka, All chemicals and reagents used were of analytical grade.

Preparation of standard stock solution

a) Metoclolpramide hydrochloride standard stock solution

An accurately weighed quantity of MET (~20 mg) was transarferred in 100.0 mL volumetric flask, dissolved in sufficient quantity of milli-Q water. The volume was made up to the mark with milli-Q water. (Concentration: 200 µg/ mL).A 5 ml portion of this solution was diluted with Milli-Q water in a 100.0mL volumetric flask up to mark to get final concentration 10µg/mL The standard solution of Metoclolpramide were scanned in the range of 200-400nm in 1.0 cm cell against solvent Milli-Q water and spectra was recorded. Absorbances of the final dilutions were scanned at 243.0, 262.0, 273.5 and 309.0 nm in 1.0cm cell against solvent using Milli-Q water.

b) Paracetamol standard stock solution

An accurately weighed quantity of PAR (~20 mg) was transferred in 100.0 ml volumetric flask, dissolved in sufficient quantity of milli-Q water. The volume was made up to the mark with water. (Concentration: 200 µg/ ml). A 5 ml portion of this solution was diluted with Milli-Q water in a 100.0mL volumetric flask up to mark to get final concentration 10µg/mL The standard solution of Paracetamol were scanned in the range of 200-400nm in 1.0 cm cell against solvent Milli-Q water and spectra was recorded. Absorbances of the final dilutions were scanned at 243.0, 262.0, 273.5 and 309.0 nm in 1.0cm cell against solvent using Milli-Q water.

Selection of Wavelength

From the standard stock solution further diluted with milli-Q Water to obtain the concentration of 10µg/ mL each solution were scanned in UV range (200-400 nm) in 1.0 cm cell against solvent blank. The overlain spectrum of drugs so recorded. The study of spectrum reveals that MET shows a well defined λ_{max} at 273.5 nm and PAR shows a well defined λ_{max} at 243.0 nm; these two wavelengths were selected for development of simultaneous equation method, 243.0 nm λ_{max} for paracetamol, 262.0 nm Isoabsorptive point for absorbance ratio method, and 309.0 for correction method.

II) Study of Beer-Lambert's law

Aliquots of standard stock solution MET and PAR were diluted in a series of 100 mL volumetric flask with milli-Q water to get concentration in range of 4-16 **µg**/mL for MET and 4-16 µg/mL for PAR Similarly standard stock solutions were appropriately mixed and diluted to get series of concentration ranging from 4-16µg/mL for MET and 4-16 µg/mL for PAR respectively. Absorbances of each of the resulting solutions were measured at 243.0 nm, 262.0 nm. 273.5 nm, and 309.0 nm in 1.0 cm cell using solvent blank. The graphs were plotted as concentration vs. absorbance for MET and PAR and their mixture respectively.

Determination of Absorptivity value

The absorbance of each of the final dilution (10µg/mL of MET and10µg/mL PAR) were measured in triplicate in 1.0 cm cell against solvent using Milli-Q water at 243.0, 262.0,273.5 and 309.0 nm respectively and A(1% 1cm) values were calculated using below formula.

$$\text{Absorptivity} = \frac{\text{Absorbance at selected wavelengths}}{A\ (1\%\ 1cm)\quad gm / 100mL\ (conc.)} \times 100$$

Procedure:

Estimation of MET and PAR in marketed formulation (Assay):

For the estimation of commercial formulation, twenty tablet of brand Metopar (Cosme Farma laboratory limited, karnataka) containing 5mg Metoclolpramide (MET) 500 mg paracetamol (PAR).Twenty tablets were weight accurately and average weight per tablet was calculated. Tablets were ground to a fine powder. A quantity equivalent to 100 mg of PAR was transferred to a volumetric flask. MET present in this tablet powder was 1 mg,which could not be found accurately due to low absorbance ; hence to increase the accuracy, accurately weight 99mg pure drug sample of MET was transfered to the the same volumetric flask. The powder was dissolved in 100 ml milli-Q water with vigorous shaking and volume was made to mark with milli-Q water. The solution was further diluted to get final concentration of 10µg/ml of PAR (or MET).

In method I, The absorbance of the solution was measured at 243.0 nm and 273.5 nm and concentration of the two drug was calculated using (Eqn.1) $Cx = A_2\, ay_1 - A_1\, ay_2 / ax_2\, ay_1 - ax_1\, ay_2$ and (Eqn.2) $Cy = A_1\, ax_2 - A_2 a\, x_1 / ax_2\, ay_1 - ax_1\, ay_2$ The result of tablet formulation are shown in Table 1. Where,

Cx and Cy are concentration in g/100 ml of MET and PAR, respectively. ax_1 is the absorptivity of MET at 243.0 nm, ax_2 is the absorptivity of MET at 273.5 nm, ay_1 is the absorptivity of PAR at 243.0 nm, ay_2 is the absorptivity of PAR at 273.5 nm.

In isoabsoptive point was employed as method II, which the absorbance was measured at two wavelength, one being the isoabsorptive point of the two components and other being the wavelength of maximum absorption of one of the two components. From the overlain spectra of two drugs absorbances were measured at selected wavelength i.e. 265.0 nm isoabsoptive point and 243.0 nm, λmax of PAR [Figure1]. The absorbance and absorptivity values at the particular wavelengths were calculated and substituted in the following equation; to obtain the concentration Cx= (Qm-Qy) /(Qx-Qy)A*ax (3) and Cy=Qm-Qx/Qy-QxA*ay (4) where, A=Absorbance of mixture at isoabsoptive point.QM=Ratio of absorbance of laboratory mixture at 243.0 nm and 262.0nm,QX= Ratio of absorptivity of MET at 243.0 nm and 262.0 nm,QY=Ratio of absorptivity of PAR at 243.0 nm and 262.0 nm.

In method III Absorbance correction method uses the absorbances at two selected wavelengths, one at λmax of one drug where other drug also shows considerable absorbance and other being the wavelength at which the first drug has practically nil absorbance.309.0 nm is the corrected wavelength. All the results of tablet formulations are shown in (TableNo. 2).

Method validation:

Validation of the proposed methods was carried out for its accuracy, precision, specificity and ruggedness according to ICH guidelines. Recovery studies were carried out at four different levels by adding the pure drug (2, 4, 6, 8, mg respectively) to previously analysed tablet powder sample. From the amount of drug found, percentage recovery was calculated (Table No.3) and linearity range also analysed at different percentage this shown in (Figure No.2)

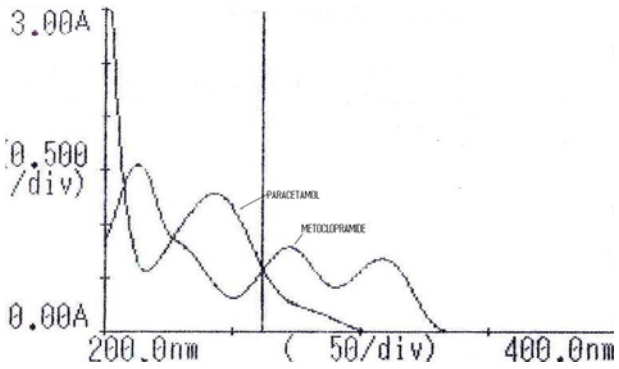

Figure1: Overlain spectra of etoclopramide and Paracetamol

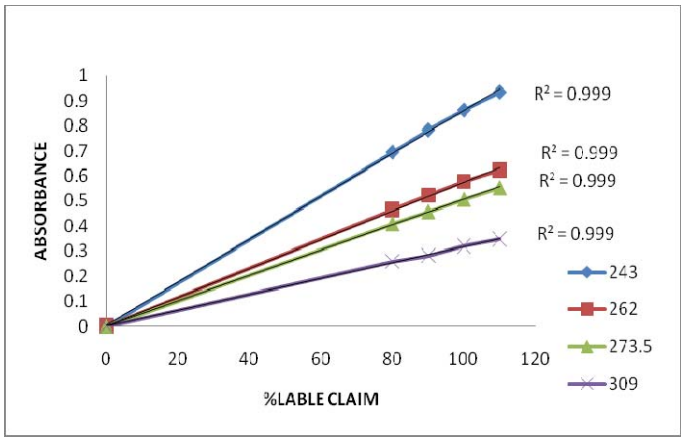

Figure 2 : Linearity and Range

Result and Discussion:

The proposed methods were found to be accurate, simple, rapid and reproducible. The two drugs follow Beer-Lambert's law over the concentration range of 4-16 µg/mL for MET and 4-16 µg/mL for PAR the values of standard deviation were found satisfactory and the recovery studies were close to 100 %. Thus all the methods can be applied in the routine analysis of the Metoclopramide and Paracetamol.

Table No.1: Validation parameter of all three methods

	Method I	**method II**	**method III**
Beer's law range			
Metoclolpramide	4-16 µg/mL	4-16 µg/mL	4-16 µg/mL
Paracetamol	4-16µg/mL	4-16µg/mL	4-16µg/mL
Wavelength (nm)	273.5 nm, 243.0 nm	262.0 nm, 243.0 nm	243.0 nm, 309.0 nm
Correlation Coeffi.	0.9999, 0.9997	0.9996, 0.9997	0.9998, 0.9997
Slope	0.037, 0.061	0.059, 0.037	0.061, 0.032
%RSD			
Intraday precision	0.0, 0.1807	0.062, 0.158	0.057, 0.16
Interday precision	1.6, 1.56	1.53, 1.59	1.57, 1.51

*in case of slope & %RSD value 1st was Metoclolpramide & 2nd was Paracetamol

Table No.2: Results of Assay by Method I, II & III

Sr. No.	Wt. taken (mg)	**% Label Claim**					
		Method (I)		Method (II)		Method (III)	
		PAR	MET	PAR	MET	PAR	MET
1	100.10	100.84	99.30	101.056	99.233	99.6145	99.597
2	100.00	101.29	98.93	101.965	98.709	101.6383	98.8204
3	100.20	101.70	99.16	100.722	99.50	101.7789	99.1116
4	99.90	100.94	98.80	101.493	98.618	100.4348	99.0390
5	100.13	101.32	99.06	101.313	99.065	100.0013	99.50
Avg.		101.223	99.084	101.31	99.025	100.69	99.2154
Std.		0.343	0.194	0.466	0.366	0.972	0.327
CV		0.33	0.19	0.46	0.36	0.96	0.33

MET - Metoclopramide & **PAR** - Paracetamol

Table No 3: Recovery studies

Sr. No.	**Amount of Pure Drug Added (mg)**		**% Recovery**					
			Method I		**Method II**		**Method III**	
	PAR	**MET**	**PAR**	**MET**	**PAR**	**MET**	**PAR**	**MET**
1	1.9	2.2	100.39	99.81	98.18	98.81	100.19	98.48
2	3.8	4.0	99.39	10031	100.28	100.86	98.91	100.34
3	6.1	6.2	98.78	99.48	99.98	97.78	99.57	99.29
4	8.2	8.0	98.79	99.87	99.79	97.15	99.57	99.29
Avg.			99.51	98.56	99.04	98.88	98.50	99.03
± SD			0.699	.0780	0.414	0.658	0.787	0.606
CV			0.69	0.76	0.41	0.65	0.77	0.59

MET - Metoclopramide & **PAR** - Paracetamol

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