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Development of UV Spectrophotometric method for the simultaneous estimation of Meloxicam and Paracetamol in tablet by simultaneous Equation, Absorbance ratio and Absorbance Correction method

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Abstract: A simple, specific, accurate, precise and reproducible method has been developed and validated for the simultaneous estimation of meloxicam 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 257.6 nm and 270.6 nm for estimation of meloxicam (MEL) and paracetamol (PAR) respectively while for Method II, 257.6 nm λ_{max} for paracetamol, 297.6 nm Isoabsorptive point of Par and Mel and 362.0 nm for correction method. The two drugs follow Beer-Lambert's law over the concentration range of 1-5 µg/mL for MET and 7-35 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 MEL 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 meloxicam and paracetamol in combined dosage form.

Keywords:- Meloxicam (MEL), Paracetamol(PAR) , UV spectroscopy, Simultaneous Equation method, Absorbance Ratio method and Correction method.

Introduction:

Paracetamol is chemically [PAR, N-(4-hydroxyphenyl) acetamide]. It is used mainly as antipyretic[1]. Meloxicam [MEL, 4-hydroxy-2-methyl-N (5-methyl-2-thiazolyl)-2-H-1,2-benzothiazine-3-carboxamide-1,1-dioxide] is used to relieve symptoms of pain and inflammation[2]. It finds its use as anti-inflammatory in this combination, the non-steroidal anti-inflammatory drug and COX-II inhibitor acts as muscle relaxant. Literature survey reveals that gas chromatography[4] HPLC[5], titrimetric[6] and densitometric methods are available for the determination of paracetamol and spectrophotpmetric[8] HPLC[7,9] ,HPTLC[10], LC[11], LC-MS[12] and Fluorimetric[13] spectroscopic method for the determination of Meloxicam. The review of literature revealed that no method is yet reported in solvent 0.1N NaOH 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 meloxaicam 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. 0.1N NaOH and Whatmann filter paper (no.41) were used throughout the experimental work.

Materials

Multicomponent tablet MELODOL (MEL 7.5mg and PAR 325.mg) manufactured by Aristo (Otsira) 23-A, shah Industrial Estate, Andheri (w) Mumbai, All chemicals and reagents used were of analytical grade.

Preparation of standard stock solution

1) Meloxicam standard stock solution

An accurately weighed quantity of MEL (~25 mg) was transarferred in 50.0 mL volumetric flask, dissolved in sufficient quantity of 0.1N NaOH. The volume was made up to the mark with 0.1N NaOH. (Concentration: 500 µg/ mL).A 1 ml portion of this solution was diluted with 0.1N NaOH in a 50.0mL volumetric flask up to mark to get final concentration 10µg/mL The standard solution of Meloxicam were scanned in the range of 200-400nm in 1.0 cm cell against solvent 0.1N NaOH and spectra was recorded. Absorbance's of the final dilutions were scanned at 257.6, 270.6, 297.6 and 362.0 nm in 1.0cm cell against solvent using 0.1N NaOH show's Overlain spectra of Meloxicam and Paracetamol (Fig. No. 1).

2) Preparation of Paracetamol Standard Solution:

An accurately weighed quantity of PAR (~25 mg) was transferred in 50.0 ml volumetric flask, dissolved in sufficient quantity of 0.1N NaOH. The volume was made up to the mark with water. (Concentration: 200 µg/ ml). A 1 ml portion of this solution was diluted with 0.1N NaOH in a 50.0mL 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 0.1N NaOH and spectra was recorded. Absorbance's of the final dilutions were scanned at 257.6, 270.6, 297.6 and 362.0 nm in 1.0cm cell against solvent using 0.1N NaOH show's Overlain spectra of Meloxicam and Paracetamol (Fig. No. 1).

Selection of Wavelength

From the standard stock solution further diluted with 0.1N NaOH 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 MEL shows a well defined λ_{max} at 362.0 nm and PAR shows a well defined λ_{max} at 257.6 nm; these two wavelengths were selected for development of simultaneous equation method, 257.6 nm λ_{max} for paracetamol, 270.6 nm Isoabsorptive point for absorbance ratio method, and 362.0 for correction method.

Study of Beer-Lambert's law

Aliquots of working stock solution of MEL and PARA were diluted with 0.1NaOH to get concentration in range of 1-5 µg/mL for MEL and 7-35 µg/mL PAR individually. Similarly standard stock solution were appropriately mixed and diluted to get series of concentration ranging from 1-5 µg/mL & 7-35 µg/mL for both MEL and PAR. Absorbances of each of the resulting solution were measured at 257.6, 270.6, 297.6, & 362.0 nm in 1.0 cm sell using solvent blank. The graphs were constructed as concentration vs. absorbance and are depicted in (Fig. No. 2).

Determination of Absorptivity value

The absorbance of each of the final dilution (10µg/mL of MEL and10µg/mL PAR) were measured in triplicate in 1.0 cm cell against solvent using 0.1N NaOH at 257.6, 270.6, 297.6, & 362.0 nm respectively and A(1% 1cm) values were calculated using below formula.

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

Procedure:

Estimation of MEL and PAR in marketed formulation:

For the estimation of commercial formulation, twenty tablet of brand MELODOL (Cosme Farma laboratory limited, karnataka) containing 7.5mg Meloxicam (MEL) 325mg 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 35 mg of PAR was transferred to a volumetric flask. MEL present in this tablet powder was 0.97 mg,which could not be found accurately due to low absorbance ; hence to increase the accuracy, accurately weight 4.3mg pure drug sample of MEL was transfered to the the same volumetric flask. The powder was dissolved in 50 ml 0.1N NaOH with vigorous shaking and volume was made to mark with 0.1N NaOH. The solution was further diluted to get final concentration of 2µg/ml of MEL and 14 µg/ml of PAR.

In method I, The absorbance of the solution was measured at 257.6 nm and 270.6 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 MEL at 257.6.0 nm, ax_2 is the absorptivity of MEL at 270.6 nm, ay_1 is

the absorptivity of PAR at 257.6 nm, ay_2 is the absorptivity of PAR at 270.6 nm.

In isoabsoptive point was employed as method II, which the absorbance was measured at two wavelengths, 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. 297.6 nm isoabsoptive point and 257.6 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 257.6 nm and 297.6 nm, QX= Ratio of absorptivity of MEL at 257.6 nm and 297.6 nm , QY=Ratio of absorptivity of PAR at 257.6.0 nm and 297.60 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.362.0 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 (1, 2, 3, 4, 5mg 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.3)

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 1-5 µg/mL for MEL and 7-35 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 Meloxicam and Paracetamol.

Table No.1: Validation parameter of all three methods

	Method I	method II	method III
Beer's law range			
Meloxicam	1-5 µg/mL	1-5 µg/mL	1-5 µg/mL
Paracetamol	7-35µg/mL	7-35 µg/mL	7-35 µg/mL
Wavelength (nm)	257.6 nm, 270.6 nm	257.6 nm, 297.6 nm	257.6 nm, 362.0 nm
Correlation Coeffi.	0.9999, 0.9997	0.9996, 0.9997	0.9998, 0.9997
	Linearity equation = y = mx+c		
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 Meloxicam & 2nd was Paracetamol

Table No.2: Results of simultaneous estimation of marketed formulation for Method I, II & III

		% Label Claim					
Sr.	**Wt.taken**	**Method (I)**		**Method (II)**		**Method (III)**	
No.	**in(mg)**	**PAR**	**MEL**	**PAR**	**MEL**	**PAR**	**MEL**
1	100.10	100.841226	99.30	101.056	99.233	99.6145	99.597
2	100.00	101.296727	98.9377	101.965	98.709	101.6383	98.8204
3	100.20	101.706342	99.1622	100.722	99.50	101.7789	99.1116
4	99.90	100.946041	98.8057	101.493	98.618	100.4348	99.0390
5	100.13	101.326398	99.0602	101.313	99.065	100.0013	99.50
	Avg	101.223347	99.0845	101.31	99.025	100.69	99.2154
	Std	0.34358528	0.19425	0.4667	0.366	0.97233	0.32775
	Cv	0.3394328	0.19611	0.46072	0.3696	0.96564	0.3303

MEL is Meloxicam and PAR is Paracetamol

Table No.3 Recovery studies

	Amt. of pure		**% Recovery**					
Sr.	**Drug added**		**Method (I)**		**Method (II)**		**Method (III)**	
	In (mg)							
No.	**PAR**	**MEL**	**PAR**	**MEL**	**PAR**	**MEL**	**PAR**	**MEL**
1	1.2	.98	100.39	99.81	98.18	98.81	100.19	98.48
2	2.5	2.3	99.39	100.31	100.28	100.86	98.91	100.34
3	3.2	3.3	98.78	99.48	97.98	98.78	99.57	99.29
4	4.4	4.1	99.79	99.87	98.79	99.15	100.48	99.6
5	5.1	5.0	98.87	99.73	101.2	98.77	100.22	98.33
	Avg		99.51	98.56	99.04	98.88	98.5	99.03
	±SD		0.699	0.78	0.414	0.658	0.787	0.606
	CV		0.696	0.769	0.409	0.651	0.776	0.599

MEL is Meloxicam and PAR is Paracetamol

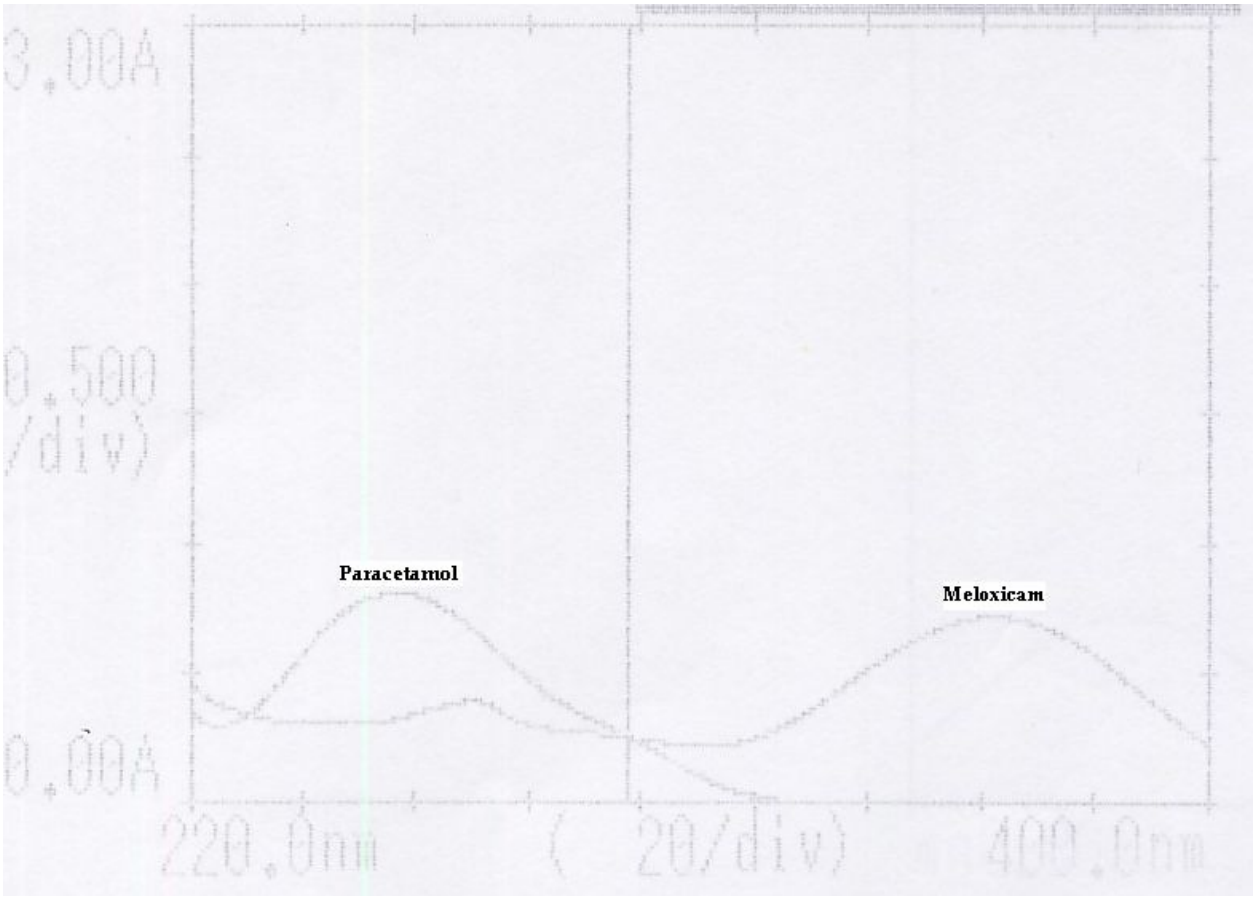

Figure1:-Overlain spectra of Metoclolpramide and Paracetamol

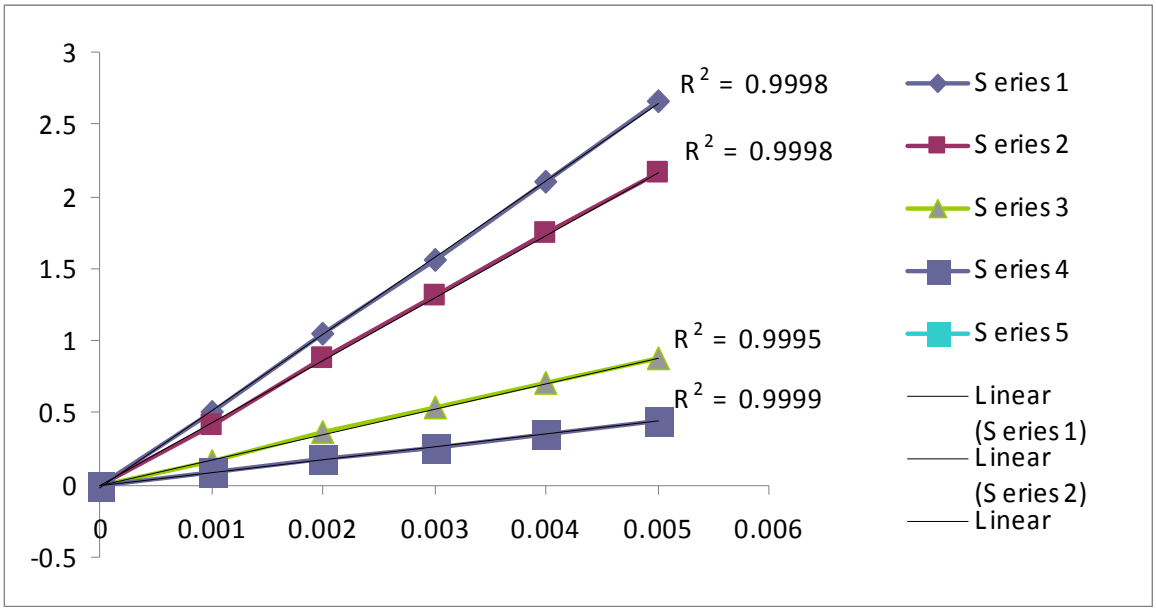

Figure 2:-Study of Beer-Lambert's law

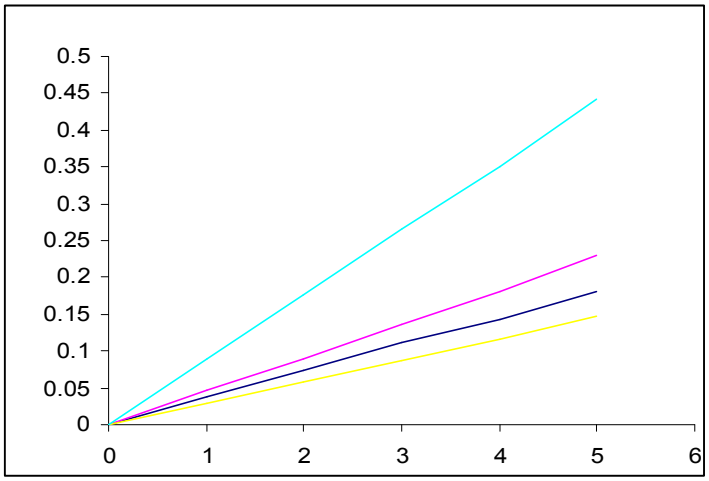

Figure 3 :- Linearity and Range

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