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Simultaneous UV Spectrophotometric Method for Estimation of Paracetamol and Nimesulide in Tablet Dosage Form

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Abstract : Paracetamol is an analgesic and antipyretic drug and Nimesulide is an non steroidal anti-inflammatory drug. simple, accurate, precise, reproducible, requiring no prior separation and economical procedures for simultaneous estimation of Paracetamol and Nimesulide in tablet dosage form have been developed. Method employs formation and solving of simultaneous equation using 245.5 nm and 299.5 nm as two analytical wavelengths for both drugs in methanol-Distilled water (50:50). Paracetamol and Nimesulide at their respective λmax 245.5 nm and 299.5 nm shows linearity in a concentration range of 1-11µg /mL and 5-30µg /mL. Recovery studies for Paracetamol 99.56 % and 100.14% for Nimesulide in case of simultaneous equation method confirming the accuracy of the proposed method. The proposed method is recommended for routine analysis since it is rapid, simple, accurate and also sensitive and specific.
Key Words: Paracetamol, Nimesulide, λmax , Simultaneous equation method.

Introduction

Paracetamol and Nimesulide are available in tablet dosage form in the ratio of 5:1. Paracetamol is N-(4 – hydroxyphenyl) acetamide ,a para-aminophenol derivative, has analgesic and antipyretic properties and weak anti-inflammatory activity. Paracetamol is official in Indian Pharmacopoeia and British Pharmacopoeia[1]B.P.The I.P.& B.P. both suggest titrimetric and UV spectrophotometric assay method for paracetamol in bulk and tablet formulations. Nimesulide is chemically it is [N-(4-nitro-2-phenoxy-phenyl)] methanesulfonamide has non steroidal anti-inflammatory drug with good analgesic and anti-rheumatic properties. It is approved for used in treatment of musculoskeletal disorder, thrombophlebitis and dental pain,inflammation.Some HPLC [2,3] and spectrophotometric [4,5] ,method have been reported in literature for it's estimation.

Many methods have been reported in literature for determination of paracetamol with other drugs individually and in combination.[6-11] However there is no UV spectrophotometric methods for study of Paracetamol and Nimesulide in tablet dosage form in pharmaceutical preparations has been found in literature survey.. The objective of the present work is to develop and validate new analytical methods for simultaneous determination of Paracetamol and Nimesulide in tablet dosage form. This communication forms the first report of simple, sensitive and reproducible methods for the simultaneous estimation of Paracetamol and Nimesulide from combined dosage form.

Materials and Methods

Materials:

Spectral runs were made on a Shimadzu UV-Visible spectrophotometer, model- 1700 (Japan) was employed with spectral bandwidth of 0.5 nm and wavelength accuracy of ± 0.3 nm with automatic wavelength corrections with a pair of 10 mm quartz

cells. Glasswares used in each procedure were soaked overnight in a mixture of chromic acid and sulphuric acid rinsed thoroughly with double distilled water and dried in hot air oven. Paracetamol and Nimesulide reference standard was kindly provided by Medico Remedias Pvt.Ltd. and Alicon Pharmaceutical Pvt.Ltd. Mumbai, respectively. The pharmaceutical preparations of combination of Paracetamol and Nimesulide that is Neulab Active (Laborate Pharmaceutical india H.P.) Methanol-distilled water (50:50) is used as solvent. All the solutions were protected for light and were analyzed on the day of preparations.

Selection of common solvent:

Methanol and distilled water (50:50) of analytical reagent grade was selected as common solvent for developing spectral characteristics of drug. The selection was made after assessing the solubility of both the drugs in different solvents.

Preparation of standard drug solution:

Standard stock solutions containing Paracetamol (PC) and Nimesulide (NM) were prepared individually by dissolving 10 mg of Paracetamol and 10 mg of Nimesulide separately in 50 ml of methanol. It was then sonicated for 10 minutes and the final volume of both the solutions were made up to 100 ml with distilled water to get stock solutions containing 100mcg/ mL each of PC and NM in two different 100 ml volumetric flasks.

Determination of absorption maxima:

By appropriate dilution of two standard drug solutions with Methanol-distilled water (50:50), solutions containing 10 µg ml^{-1} of PC and 10 µg ml^{-1} of NM were scanned separately in the range of 200- 600 nm to determine the wavelength of maximum absorption for both the drugs. PC and NM showed absorbance maxima at 245.5 nm (λ_1) and 299.5 nm (λ_2) respectively.

Simultaneous Equation Method:-

Two wavelengths selected for the method are 245.5 nm and 299.5 nm that are absorption maximas of PC and NM in Methanol-Distilled water (50:50) solutions respectively. The stock solutions of both the drugs were further diluted separately with Methanol-Distilled water (50:50) to get a series of standard solutions of1-11µg /mL concentrations of Paracetamol and 5-30µg /mL concentrations of Nimesulide.The absorbance were measured at the selected wavelengths and absorptivities (A 1%, 1 cm) for both the drugs at both wavelengths were determined as mean of six independent determinations. Concentrations in the sample were obtained by using
following equations-

$$Cx = \frac{A1\ ay2 - A2\ a\ y1}{ax1ay2 - ax2ay1} \quad \text{..... Eq. (i)}$$

$$Cy = \frac{A1\ a\ x2 - A2\ a\ x1}{a\ y1ax2 - ay2a\ x1} \quad \text{.....Eq. (ii)}$$

Where, A1 and A2 are absorbances of mixture at 245.5 nm and 295.5 nm respectively, ax1 and ax2 are absorptivities of PC at λ_1 and λ_2 respectively and ay1 and ay2 are absorptivities of NM at λ_1 and λ_2 respectively. Cx and Cy are concentrations of PC and NM respectively.

Application of the Proposed Method for the Determination of PC AND NM in Tablets:

Marketed tablet formulation containing paracetamol 500 mg and nimesulide 100 mg was analyzed using this method. From the 20 tablets, an amount equivalent to 500 mg of paracetamol and 100 mg of nimesulide was weighed and from that the amount equivalent to 50mg of paracetamol and 10 mg of nimesulide was weighed and dissolved in 50 ml of methanol and sonicated for 10 minutes. Then the volume made upto 100ml with distilled water to get a stock solution containing 100mcg/mlof nimesulide and 500mcg/ml of paracetamol. Then the solution was filtered through Whatman filter paper no. 41. Appropriate aliquots of paracetamol and nimesulide within the Beer's law limit were taken. The absorbances of resulting solutions were measured at 245.5 nm and 299.5 nm. The concentration of paracetamol and nimesulide present in the sample solution was calculated by using the equation generated from calibration curve of respective drugs.In this method the concentration of both PC and NM were determined by measuring the absorbance of the sample at 245.5 nm and 299.5 nm. Values were substituted in the respective formula to obtain concentrations.

Validation:

The method was validated according to ICH Q2B guidelines for validation of analytical procedures in order to determine the linearity, sensitivity, precision and accuracy for the analyte.

Accuracy:

To ascertain the accuracy of the proposed methods, recovery studies were carried at three different levels (80%, 100% and 120%). Percent recovery for PC and NM ,by this methods, was found in the range of 99.56-100.14%

Linearity:

The linearity of measurement was evaluated by analyzing different concentration of the standard solution of PC and NM. For simultaneous equation

method the Beer- Lambert's concentration range was found to be for1-11 µg/ml for PC and 5-10 µg/ml NM.

Results and Discussion

The overlain spectra of PC and NM exhibit λ max of 245.5 nm and 299.5 nm for PC and NM respectively which are quite separated from each other. Standard calibration curves for PC and NM were linear with correlation coefficients (r) values in the range of 0.9996- 0.9999 at all the selected wavelengths and the values were average of six readings with standard deviation in the range of 0.6244-0.7810. The calibration curves were repeated three times in a day and the average % RSD was found to be 0.6294 for PC and 0.1578 for NM. The accuracy of the method was conformed by recovery studies from tablet at three different levels of 80 % , 100 %, 120 % ; recovery in the range of 99.56-100.14% justifies the accuracy of method.

Conclusion

The most striking feature of this method is its simplicity, economy and rapidity, non- requiring-consuming sample preparations such as extraction of solvents, heating, degassing which are needed for HPLC procedure. These are new and novel methods and can be employed for routine analysis in quality control analysis. The described methods give accurate and precise results for determination of Paracetamol, and Nimesulide mixture in marketed formulation.

Table 1: **Linear regression analysis of calibration curves with their respective absorptivity values**

Parameter	**Simultaneous equation method**	
	PC	**NM**
Working λ (in methanol :water 50:50)	245.5	299.5
Beer Lamberts Law range	1-11 µg/ml	5-30 µg/ml
Molar absorptivity (lit/mole/cm)	12070.0780	7600.281918
Sandell's sensitivity (mcg/Sq.cm/0.001)	0.012527	0.040566
Slope	0.079829 (at 245.5), 0.004114 (at 299.5)	0.024651 (at 299.5) 0.027949 (at 245.5)
Regression coefficient(r^2)	0.9998(at 245.5) 0.9998 (at 299.5)	0.9999(at 299.5) 0.9997 (at 245.5)
LOD	0.3347	0.08032
LOQ	0.9639	0.2433

Table 2: Results of analysis of tablet samples.

Drugs	Label claim	Amount Found	% label claim	S.D.*	R.S.D.*	%Recovery*
PC	500	495	99.0	0.6244	0.6294	99.56
NM	100	92.2	99.2	0.7810	0.1578	100.14

* indicates mean of six determinations.

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