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Research article

Development and validation of spectrophotometric method with hydrotropic solubilizing agent for simultaneous estimation of domeperidone and paracetamol in solid dosage form

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ABSTRACT

A simple, precise and UV-Visible spectroscopic method was developed and validated for simultaneous estimation of domeperidone an anti emetic and paracetamol an NSAID'S in solid dosage form" The identification of both drugs was achieved on 8 M Urea solution as a suitable solvent in all temperature , Absorbance of the sample solutions at 287.0 nm and 248.0 nm was measured and from the appropriate absorbance values, Both domeperidone and paracetamol obey Beer's law in the concentration range of 10-50 µg/ml. the concentration of drugs in the sample solution was determined by using Vierodt's formula. The method was successfully validated in accordance to ICH guidelines. Values of accuracy, precision and other statistical analysis were found to be in good according with the standard values. Further, the validated method was applied for commercially available pharmaceutical dosage form.

Keywords: Validation, Simultaneous, Solubilization, ICH guideline, spectroscopy.

INTRODUCTION

Hydrotrophy is a solubilization phenomenon whereby addition of large amount of a second solute results in an increase in the aqueous solubility of another solute. Generally hydrotropic agent is hydroxybenzoate, Sodium salicylate Nicotinamide, Sodium glycinate, Ascorbic acid, Dimethyl urea, Sodium salt of Ibuprofen, , Sodium ascorbate, hydrochloride salt of metformine, 2 M Sodium Benzoate, 2 M Niacinamide, 4 M Sodium Acetate, 8 M Urea and 1.25 M Sodium Citrate. For Domperidone (figure 1) is antiemetic an agent and Paracetamol (Fig.2) is an NSAID's agent. Paracetamol 5-chloro-1-[1-[3-(2, 3-dihydro-2-oxo-1H-benzimidazol-1-yl) propyl] piperidin-4-yl]-2,3-dihydro-1H-benzimid azol-2-one, Domperidone is generally used for disorders of the gastrointestinal tract (gut). UV-Visible spectroscopy (1-3), Derivative Spectro photometry absorbance Ratio Spectroscopy (4-6), HPTLC and HPLC (7-1-) methods are reported for simultaneous estimation of Paracetamol in combined dosage form. No one any method has been reported for the estimation of Paracetamol (DPD) and Paracetamol (PCM) in combined dosage form and analysis by using hydrotropic solubilization technique. Present work indicating on the quantitative estimation of Paracetamol and Paracetamol in their combined dosage form hydrotropic solubilization [1].

MATERIAL AND METHOD

Instrument

There experimental work was carried out Shimadzu (model UV-1700 Pharmaspec series) UV-visible spectrophotometer, having double beam detector configuration with 1 cm matched quartz smple cells, centrifuge, Cyclo Mixer, ultrasonicator, magnetic stirrer apparatus were used [2].

Commercial Formulation & standards

Reference standard of Paracetamol and Paracetamol was gift from Lupin pharmaceutical pvt. Ltd., Mandideep, Bhopal (India).

Urea was obtained from Loba chem, Mumbai. Commercial tablets marketed combination of paracetamol (20mg) and paracetamol (500mg) is Grenil, from Scon Pharmaceutical Limited, Indore (India).

Determination of Solubility

Solubility of Paracetamol and Domperidone was performed in different solvents and result was shown in (Table No.1).

Table 1: - Solubility of Domperidone & Paracitamol

Solvent	Domperidone	Paracitamol
Water	Sparingly Soluble	Sparingly soluble
0.1 N HCl	Sparingly Soluble	Sparingly soluble
Methanol	Soluble	Freely soluble
Ethanol	Soluble	Freely soluble
0.1 N NaOH	Slightly soluble	Freely soluble

Selection of Hydrotropes for Poorly Water-Soluble Drugs

Distilled water was used in making hydrotropic solutions. 2 M Sodium Benzoate, 2 M Niacinamide, 4 M Sodium Acetate, 8 M Urea and 1.25 M Sodium Citrate were employed as hydrotropic solutions. 25 ml of distilled water/hydrotropic solution was taken in a 50 ml glass bottle and gross weight (including the cap) was noted. Then, few mg (by visual observation) of fine powder of drug was transferred to the bottle. The bottle was shaken vigorously (by hand). When drug got dissolved, more drugs (few mg by visual observation) were transferred to the bottle and again the bottle was shaken vigorously. Same operation was repeated till some excess drug remained undissolved (after constant vigorous shaking for 10 minutes). Then, again gross weight was noted. From the difference in two readings (of weight), an approximate solubility was determined and solubility enhancement ratios were calculated for all selected drugs for all six hydrotropic solutions. When the determined solubility enhancement ratio was at least 5, such hydrotropic solution was selected for that drug (Table No.2) [3].

Table 2: Selection of Hydrotropes for Poorly Water-Soluble Drugs

Drug	Selected Hydrotropic Solution
Domperidone	8 M Urea
Paracetamol	8 M Urea

Determination of Interference of Hydrotropic Agents

A UV-Visible Spectrophotometer with 1 cm matched silica cells was employed for spectrophotometric determinations. For determination of interference of hydrotropic agents in the spectrophotometric estimation of Paracetamol and Domperidone, the absorbances of the standard solutions of drugs were determined in distilled water alone and in the presence of the maximum concentration of the hydrotropic agent employed for spectrophotometric analysis/formulation purpose in the present investigation.

Estimation of drug

Method 1 - employing simultaneous

Determination of λ_{max} of drugs

Standard solution (10µg/ml) of pure Paracetamol and Domperidone was prepared. Which showed maximum absorbance at 287.0 nm and 248.0 nm for Domperidone and Paracetamol respectively. The UV spectra are shown in (Figure 1 and 2).

Figure 1: Determination of λ_{max} of Domeperidone

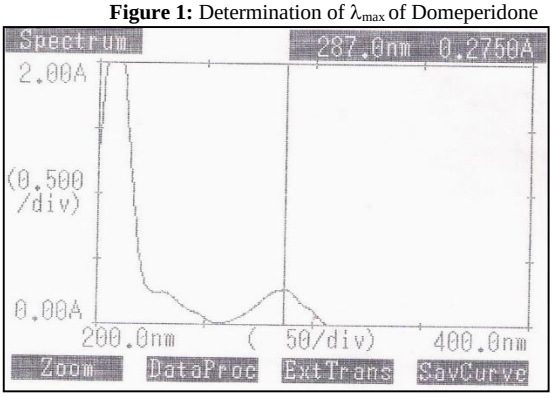
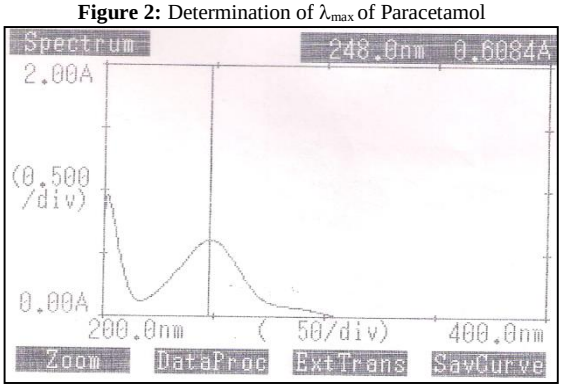


Figure 2: Determination of λ_{max} of Paracetamol



Preparation of Standard Stock Solution

An accurately weighed powder sample equivalent to 100 mg of Domperidone was transferred to 100 ml of volumetric flask containing 20 mL 8 M urea solution. The flask was sonicated for about 20 min to solubilize the drug and the volume was made up to mark with distilled water and get concentration 1000 µg mL^{-1}. An accurately weighed powder sample equivalent to 100 mg of Paracetamol was transferred to 100 ml of volumetric flask containing 20 mL 8 M urea solution. The drug and the volume was made up to mark with distilled water and get concentration 1000 µg mL^{-1} [4].

Preparation of Working Standard Solution

From the filtrate stock solution of Domperidone taking 1 mg/ml and further diluted with distilled water to get concentration of 100 µg/ ml. Taking 1 mL from working standard solution 100 µg /ml and further diluted with distilled water to get concentration range 10, 20, 30, 40, 50 µg/ ml was analyzed on UV spectrophotometer. From the filtrate stock solution of Paracetamol taking 1 mL^{-1} and further diluted with distilled water to get concentration of 100 µg/ ml. Taking 1 mL from working standard solution 100 µg mL^{-1} and further diluted with distilled water to get concentration range 10, 20, 30, 40, 50 µg/ ml was analyzed on UV spectrophotometer [5].

Preparation of the Calibration Curve of the Drugs

Each of the standard drug solutions were scanned 3 times and the mean absorbance of drug a typical calibration curve for Domperidone and Paracetamol respectively were obtained.

Preparation of Analysis of Tablet Formulation

Tablet powder equivalent to 100 mg Domperidone and Paracetamol was weighed and transferred to a 100 ml volumetric flask. Twenty mL of 8 M Urea solution was added and drug was dissolved in this solution. After complete dissolution of drug, sufficient distilled water was used to make up the volume. Resultant solution was filtered through Whatmann filter paper No 41. 1 ml of filtrate was taken in 10 ml volumetric flask and volume was made up to 10 ml with diluent to obtain concentration of 100 µg/ml. Further 5 ml of this solution was taken and diluted up to 10 ml obtain final concentration of 50 µg/ml. Absorbance of the sample solutions at 0287.0nm and 248. nm was measured and from the absorbance values, the concentration of drugs in the sample solution was determined by using Vierodt's formula. The contents were calculated using the following equations.

$$C X = \frac{(A\ 2\ ay\ 1 - A\ 1\ ay\ 2)}{(ax\ 2\ ay\ 1 - ax\ 1\ ay\ 2)}$$

$$C Y = \frac{(A\ 1\ ax\ 2 - A\ 2\ ax\ 1)}{(ax\ 2\ ay\ 1 - ax\ 1\ ay\ 2)}$$

where C_X and C_Y are the concentrations of Domperidone and Paracetamol respectively, a_{x1} and a_{x2} are the absorptivity values of Domperidone at 287.0 nm and Paracetamol at 248.0 nm respectively, ay_1 and ay_2 are the absorptivity values of Domperidone at 287.0 nm and paracetamol at 248.0 nm respectively and A_1 and A_2 are the absorbances of the diluted sample at 287.0 nm and at 248.0 nm respectively.

Where,

A_1	=	Absorbance of sample solution at 287nm
A_2	=	Absorbance of sample solution at 248 nm
Cx	=	Concentration of Domperidone in g/liter in sample solution
CY	=	Concentration of Paracetamol in g/liter in sample solution.

After obtaining the recorded absorbances, A_1 and A_2 and substituting the values concentration of each drug can be calculated.

Validation

The method validation parameters like linearity,precision, accuracy, repeatability, limit of detectionand limit of quantitation were checked as per ICH guidelines.

Linearity and Range

Linearity of analytical procedure is its ability (within a given range) to obtain test, which are directly proportional to absorbance of analyte in the sample. The calibration plot was constructed after analysis of six different (from 10 to 50µg/ml and 10to 50 µg/ml).

Precision and Accuracy

The precision of the method was evaluated by interday and intraday variation studies. In intradaystudies, working solutions of standard and sample were analysed thrice in a day and percentage relative standard deviation (% RSD) was calculated. In the inter day variation studies,working solution of standard and sample wereanalysed on three consecutive days and percentage relative standard deviation (% RSD) was calculated [6].

Method 2: employing absorbance ratio method (Q-analysis)

Q-absorbance method uses the ratio of absorbance at two selected wavelengths, one at iso-absorptive point and other being the λ_{max} of one of the two components. The standard stock solution and calibration curve were prepared at described in method 1. From the overlay spectra of Paracetamol (10 µg/ ml) and Domperidone (2 µg/ ml), two wavelengths 273.0 nm (isoabsorptive point) and 287.0 nm (λ_{max} of Domperidone) were selected for the formation of Q-absorbance. The absorbances of Paracetamol and Domperidone 273.0 nm (isoabsorptive point) and λ_{max} of Domperidone at 287.0 nm respectively and the absorptivity coefficients of each drug at both wavelengths were determined.

$$CDOM = \frac{Qm - Qy}{Qx - Qy} \times \frac{A1}{ax1} \qquad \text{Equestion (1)}$$

$$CPARA = CDOM - \frac{A1}{ax1} \qquad \text{Equestion (2)}$$

Where, A1 and A2 are the absorbances of mixture at 273.0 nm and 287.0 nm, and ax1, ax2 and ay1, ay2, are absorptivities of Domperidone at 273.0 nm and 287.0 nm respectively and $Qx = ax_2 / ax_1$, $Qy = ay_2 / ay_1$, and $Qm = A_2 / A_1$

Validation

The method validation parameters like linearity,precision, accuracy, repeatability, limit of detectionand limit of quantitation were checked as per ICH guidelines.

Linearity and Range

Linearity of analytical procedure is its ability (within a given range) to obtain test, which are directly proportional to absorbance of analyte in the sample. The calibration plot was constructed after analysis of six different (from 10 to 50µg/ml and 10to 50 µg/ml) concentrations and absorbances for each concentration were recorded three times, and mean absorbance was calculated [7].

Precision and accuracy

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DISCUSSION

Solubility of drug's in Table no. 1 shows the solubility of domeperidone and paracetamol in different solvents, methanol and ethanol 0.1 N Hcl, 0.1 N NaoH was selected for the solubility of drug because it is economical and it is easily available. Fig. 1, 2, Shows

the scanning result of Pure API's of domeperidone and the λ_{max} was found to be 287 nm and 248 nm respectively Shows the standard curve of domeperidone and patracetamol Regression equation was found from that standard curve, R^2 value is 0.997 for Domeridone and 0.997 for Paracetamol so it is Linear. Shows the optical characteristics of pure domeperidone and paracetamol the result of Analysis of Marketed Tablet formulations, the RSD of the Average of 3 determinations was found to be below 1. So that method can be used for the simultaneous estimation of Domperidone and Paracetamol from its Tablet dosage form.

CONCLUSION

The aim of these study are develovement of ecofriendly, economic and most presise method for estimation of poorly water soluble drugs compare to conventional spectroscopic estimation of drugs. These method have less cost due to uses of hydrotropic solvent in place of organic solvents.These method are used in different formulations i.e. injections.Order of observed solubility of drug in hydrotropic agents was found to be in following order: urea > sodium benzoate>sodium citrate> niacinamide > propylene glycol. Solubility in mixed solubilizers were carried out in order to decrease the individual concentration of hydrotropic agents used (to reduce the toxicity potential). Thus this spectroscopic method can be applied for routine analysis of Domperidone and Paracetamol.

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