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DEVELOPMENT AND VALIDATION OF MISOPROSTOL IN 0.1N HCL BY USING UV-SPECTROPHOTOMETRIC METHOD IN BULK FORM

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ABSTRACT

Objectives: The present study main objective is to evolve and validate stability indicating rapid, easy, economical and specific UV spectroscopic method for the estimation of misoprostol in bulk form which was used as NSAID related ulcers treatment. **Materials & Methods:** Only the Bulk form are used in this method development 0.1N HCL is used as a solvent for this study after several pre-solubility tests and several dilutions are made for the results evaluation. ELICO-Double beam SL-120/UV spectrophotometer is used for the validation and method development under certain specifications. Predicated on the physical parameters and solubility of the misoprostol, solution of standard stock of the drug was composed and absorbance maxima were set on. The wavelength maxima of misoprostol occurs at 281nm. The linearity is done by preparing the solutions from 2-10 µg/ml. The study done for the development and validation is according to Q3D guidelines which are framed in ICH. **Results:** At a certain concentration the maximum absorbance, linearity of the compound is obtained by obeying Beers law. The correlation coefficient of the drug is below 1.The limit of detection & limit of quantification of misoprostol was found to be 0.656 µg/ml and 1.988 µg/ml. Accuracy and precision of the method is within the acceptance range after by recovery studies. **Conclusion:** By the interpreted results of various validated parameters, it is concluded that the developed method

is rapid, simple, cost-effective method and suitable for quantitative determination of misoprostol in bulk form.

KEYWORDS: Misoprostol, Spectroscopy, Materials and Methods, Method development.

INTRODUCTION

Misoprostol is used as an anti-ulcer drug, which is used to protect the stomach lining and decrease stomach acid secretion acid secretion. It is primarily used to prevent ulcers due to non steroidal pain medication. This medicine can cause uterine contraction and is sometimes used for labor inducation and termination of pregnancy. The IUPAC name is 7-[(1R, 2R, 3R)-3-hydroxy-2-(4-hydroxy-4-methyloct-1-enyl)-5 oxocyclopentyl] heptanoic acid methyl ester.[1] The molecular formula of misoprostol is $C_{22}H_{38}O_5$. The Melting point of misoprostol is 261-263^{0}C and it is available in the light yellow solid form. It is soluble in DMSO, Ethanol, 0.1N HCL, NaOH, water and insoluble in chloroform.

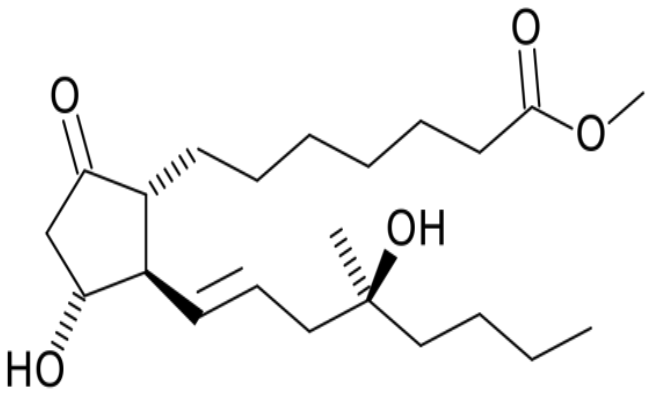

Fig. 1: Structure of misoprostol.[2]

Purity of misoprostol is 98%. Zitotec is the brand name of misoprostol. The storage room temperature of misoprostol is 25^{0}C.

Misoprostol stimulates E1 prostaglandin receptor present on the stomach parietal cells to prevent secretion of gastric acid. It is a prostaglandin E1 synthetic analog.[3] Misoprostol also induces the effects of uterotonic caused by prostaglandin i.e it causes dilation of uterus during labour and cervical opening.[4,5] The uterotonic properties helps in reduction of postpartum bleeding.

MATERIALS AND METHODS

Drug sample, Chemicals, Solvents: The drug misoprostol was brought from the Aurbindo Pharmaceuticals private limited, Hyderabad as a gift sample. From the solubility studies, the drug is mostly soluble in 0.1N HCL. Hence 0.1N HCL is used as a solvent for this developed method.

Equipments

Equipments used for the study were

1. Weighing balance with the model name of WENSAR weighing scales limited.
2. UV-VISIBLE spectrophotometer having model name of ELICO-Double beam SL-210 containing a pair of quartz cells with pathlength of 10mm.

Composition of solutions

Composition of solution containing stock 1:

To prepare a solution of 1000µg/ml concentration take 100ml volumetric flask in that add accurately weighed 100mg of misoprostol and dilute with 0.1N HCL.

Composition of solution containing stock 2:

To compose a concentration 10µg/ml, from the above stock-1 solution pippette out 1.0ml in 100ml volumetric flask and dilute with 0.1N HCL

Composition of solution containing stock 3:

To prepare a concentration of 100µg/ml solution, measure 1.0ml in 10ml volumetric flask and dilute with 0.1N HCL.

Composition of solution containing 0.1N HCL:

Pipette out 8.3ml of concentrated HCL in 1000ml volumetric flask containing 500ml distilled water and make up the volume upto the mark 1000ml with distilled water.

Methodology

Method development

Predicated on the physical parameters and solubility of the misoprostol, solution of standard stock of the drug was composed and absorbance maxima were set on. The wavelength maxima of misoprostol occurs at 281nm.[6]

Depend on the wavelength maxima (λ max) of the misoprostol, solutions of unlike concentrate were composed.

Choice of solvent

As per the Indian pharmacopeia standards, the misoprostol solubility was done in wide amounts of solvents. Misoprostol solubility is determined in a variety of solvents.[7] Based upon the solubility profile, the drug misoprostol is soluble in 0.1N HCL, Hence 0.1N HCL is used as a solvent for this developed method.

Determination of λ max

In order to prepare the concentration of 10 µg/ml solution, stock standard drug solution was diluted with 0.1 N HCL. UV range of solution scanned between 200-400nm with 0.1N HCL as blank. The drug shows maximum absorbance at 281nm. Hence the wavelength of 281nm is selected for this method. The UV spectra of misoprostol was mentioned in figure 2.

Method validation

Linearity

Linearity test was evaluated by measuring the absorbance value of solutions of standards. The stock standard solutions of different concentrations was composed and graph was plotted based on the absorbance value obtained. The wavelength maxima of unlike concentration solutions were obtained at 281nm with blank. The solutions of different concentration of 2-10µg/ml were composed. from the data of calibration curve ,concentration v_s absorbance is plotted and are found to be linear. The figure of calibration curve of misoprostol was mentioned in figure 3.

Composition of solution containing 2µg/ml solution

To compose a concentration 2µg/ml pipette out 1ml from stock 3 solution in 50ml volumetric flask and dilute with 0.1N HCL.

Composition of 4µg/ml solution

To compose a concentration 4µg/ml pipette out 2ml from stock 3 solution in 50ml volumetric flask and dilute with 0.1N HCL.

Composition of 6µg/ml solution

To compose a concentration 6µg/ml pipette out 3ml from stock 3 solution in 50ml volumetric flask and dilute with 0.1N HCL.

Composition of 8µg/ml solution

To compose a concentration 8µg/ml pipette out 4ml from stock 3 solution in 50ml volumetric flask and dilute with 0.1N HCL.

Composition of 10µg/ml solution

To compose a concentration 10µg/ml pipette out 5ml from stock 3 solution in 50ml volumetric flask and dilute with 0.1N HCL.

Precision

In this method, for the determination of precision misoprostol drug solution is composed and analysed for six times of same concentration of dissimilar two days. The relative standard deviation (%) and relative error (%) was occur within the acceptance limits of below 2, the developed method was designated with high accuracy and precision. The results of precision was tabulated in table 1.

Composition of 6µg/ml stock solution

To compose a concentration 6µg/ml pipette out 3ml from stock 3 solution in 50ml volumetric flask and dilute with 0.1N HCL.

Ruggedness

The degree of reproducibility of results obtained under a variety of conditions such as different laboratories, analysts, instruments. The results of ruggedness was tabulated in the table 2.

Composition of 6µg/ml stock solution

To compose a concentration 6µg/ml pipette out 3ml from stock 3 solution in 50ml volumetric flask and dilute with 0.1N HCL.

Limit of detection & limit of quantification

The LOD & LOQ concentration of misoprostol was detected and determined from the standard curves was 0.653µg/ml &1.988µg/ml. The uv optical characteristics of misoprostol is mentioned in table 3.

RESULTS AND DISCUSSION

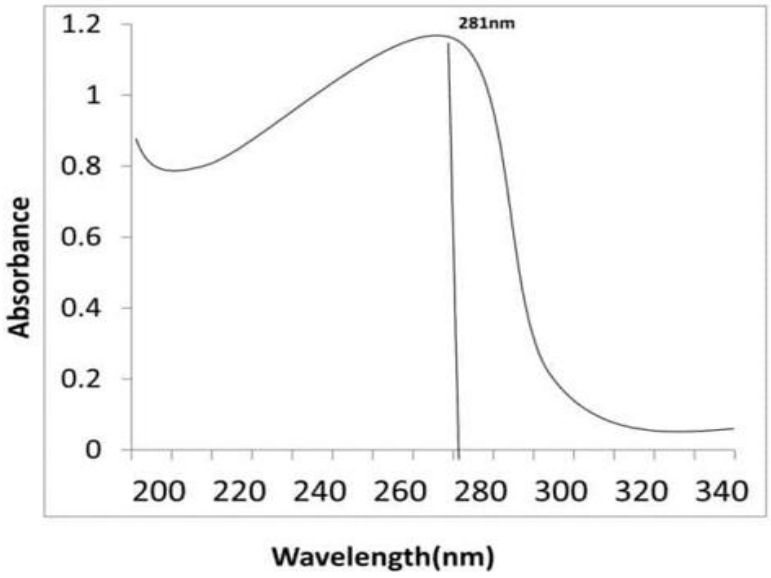

Fig. 2: Misoprostol UV spectra at 281nm.

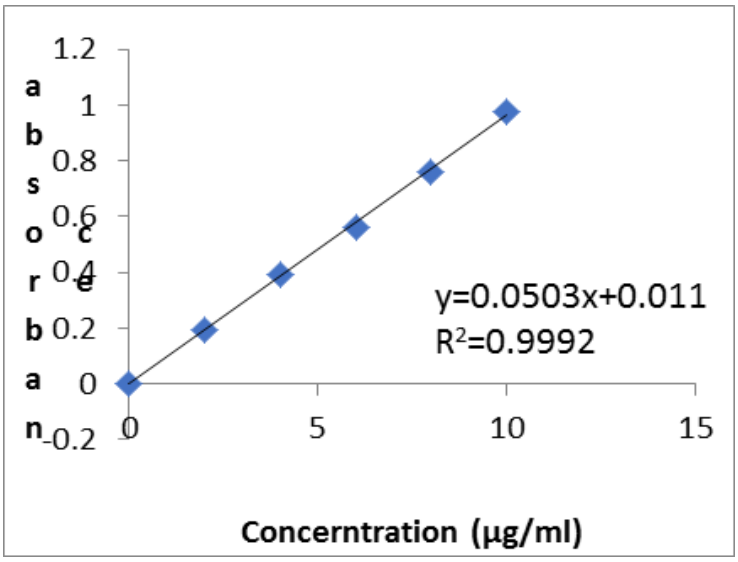

Fig. 3: Misoprostol calibration curve.

Precision

Table 1: Misoprostol precision result.

Precision	%RSD
Intraday precision	1.5
Inter day precision	1.5
Repeatability	1.26

Table 2: Misoprostol ruggedness result.

Parameter	%RSD
Ruggedness	0.47

Table 3: Misoprostol UV Optical characteristics.

Parameters	Method values
absorbance λ (nm)	281nm
Beer's law limit (µg/ml)	2-21µg/ml.
Sandell's sensitivity (µg/cm^2/0.001AU)	0.019
Molar absorbtivity (L mol-1 cm-1)	1.89x10^{14}
Correlation co-efficient (r^2)	0.9992
Slope (m)	0.0503
Intercept (c)	0.011
Regression equation (Y=mx+c)	Y=0.0503x +0.011
Standard error of mean of regression line	0.001543
LOD(µg/ml)	0.653
LOQ(µg/ml)	1.988

The misoprostol solubility was carried out in a wide amounts of solvents. Misoprostol solubility is determined in a variety of solvents. Based upon the solubility profile, the drug misoprostol is soluble in 0.1N HCL, Hence 0.1N HCL is used as a solvent for this developed method.The linearity was determined from the solution containing concentrations of 2-10 µg/ml and R^2 value was found to be below 1.This method is evaluated for the validation parameters like precision, linearity ruggedness, LOQ and LOD and results are shown in table form. The results are obtained as per ICH guidelines within the acceptance criteria. hence this developed method can be as reference for future analytical studies.

CONCLUSION

This method is evaluated and validated as per ICH guidelines. A rapid, simple, economical, precise, accurate UV spectroscopic method developed for the quantitative estimation of misoprostol in bulk form.

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