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DEVELOPMENT OF SIMPLE AND VALIDATED METHOD FOR THE QUANTITATIVE ESTIMATION OF MESALAMINE USING UV SPECTROSCOPIC METHOD

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ABSTRACT

Mesalamine is used to treat inflammatory bowel diseases including ulcerative colitis (or) inflamed anus (or) rectum and to maintain remission in crohn's diseases. Mesalamine is a newer skeletal muscle relaxant and is used along with rest and physical therapy to decrease muscle pain and spasms associated with strains, sprains or other muscle injuries. A precise, accurate, cost effective, sensitive and simple UV- Spectroscopic method has been developed for the determination of mesalamine in bulk and pharmaceutical dosage forms. The solubility of Mesalamine was determined in a variety of solvents ranging from non polar to polar. The drug was found more soluble in methanol and HCl. For the cost effective manner and since the drug is stable in HCl for long time than in methanol, (3hrs). So 1N HCl was selected as solvent. The mesalamine shows absorbance at 303 nm in 1 N HCl and it obeys Beer's law in the concentration range of 5 – 25 µ/ml. With a correlation coefficient (r^2 - 0.0993), the results of analysis were validated by recovery studies. The method was successfully feasible to pharmaceutical formulation, because no interference from the tablet exceipents were found. The proposed method was found to be simple accurate and reliable for routine quantification of mesalamine in bulk form and pharmaceutical dosage form.

KEY WORDS: mesalamine, UV spectroscope, Tablets, Precision.

INTRODUCTION

Chemically mesalamine is a 5-amino 2-hydroxy benzene 2- carboxylic acid (or) 5-amino salicylic acid (ASA). Mesalamine mainly used as an anti inflammatory agent and ulcerative colitis by inhibiting the cyclooxygenase enzyme. Mucosal production of arachidonic acid metabolites both cyclooxygenase and lipoooxygenase path ways is increased in patients with chronic inflammatory bowel diseases and it is possible that mesalamine inhibit the inflammation by blocking cyclooxygenase and inhibiting prostaglandin production in the colon.

In addition to its conversion of prostaglandins cyclooxygenase path way, arachidonic acid is converted via lipoooxygenase path way. Mesalamine is used to diminish the inflammation by blocking the synthesis of the prostaglandins.

Inhibition of COX-1 mediated synthesis of gastro protective the prostaglandins is clearly involved through local action inducing back diffusion of H^+ ions in gastric mucosa so mesalamine is mainly used for the ulcerative colitis.

Because of its versatility UV- spectroscopy is always preferred at small scale industries. Literature survey includes very few methods of UV spectroscopic methods for the estimation of mesalamine or in-combination with other drugs in bulk and pharmaceutical dosage form. It was planned to determine mesalamine by a different UV method to improve the analytical profile.

Hence the main objectives of present work was to develop and validate simple, precise, accurate, robust and cost effective UV spectroscopic method for the estimation of mesalamine in bulk and pharmaceutical dosage form as per ICH guidelines.

MATERIALS AND METHODS

Selection of solvent

A number of trails were made to find out the ideal solvent system for dissolving the drug. The solvents such as water, HCl, NaOH, methanol, Ethanol, chloroform, Benzene, Carbon tetra chloride, Glacial acetic acid are used to determine the solubility of the mesalamine. The drug is effectively soluble in 1N HCl and it shows better absorption maximum at 303 nm so it is selected as a solvent.

Instruments used

Thermo double beam UV spectrophotometer was used to record the absorption spectra. Spectrophotometer with 1 cm matched quartz cells were used for the estimation of the mesalamine.

Reagents Materials

The API i.e.; mesalamine is supplied by Hetero drugs Ltd, Hyderabad, Telangana, India. Pharmaceutical formulations like Wallace tablets which containing 400 mg of drug are obtained from local pharmacy. 1N HCl was used as a solvent during the experiment.

Selection of Wave Length

In UV absorption maximum method, a solution 10 µg/ml was scanned in UV range of 200-400nm utilizing thermo double beam UV spectrophotometer utilizing 1N HCl as blank. It was observed that the drug showed maximum absorbance at 303 nm and was selected as the detection wave length for the determination of mesalamine.

Preparation of Standard Drug Solution

100 mg of pure drug was weighed and taken in to 100 ml volumetric flask and make up the volume up to the mark with 1N HCl to get stock solution [100µg / ml]. This solution was used for further dilutions to get working standards.

Preparation of Calibration Curve

A calibration curve was constricted with the above stock solution. This solution is taken into series of 10 ml volumetric flask and up the volume up to the mark with 1N HCl in the concentration range 5-25 µg / ml and it is used to determine the absorbance at 303 nm. The absorbance values are noted in the T**able 1.** By using these values correlation coefficient (r^2= 0.9993), slope (m=0.09097), intercept(c=0.00515) were calculated and shown in T**able 2.** Calibration curve was plotted by taking mesalamine concentration on X-axis and absorbance values on Y-axis. The calibration curve is shown in the following **Figure3.**

Procedure for Assay of Marketed Tablets

20 Tablets of Marketed formulations were weighed and powdered. The tablet powder is weighed which equal to 400mg of mesalamine and transferred in to 100 ml volumetric flask and make up the volume up to the mark with 1N HCl. This solution is used for further

dilutions and scanned over 200- 400nm. The maximum absorbance was measured at 303 nm and the amount of mesalamine was computed from its Calibration plot.

Validation of developed method

Linearity

Linearity of an analytical produce is its ability (within a given range) to obtain test results which are directly proportional to the concentration of analyte in the sample. Linearity can be determined by using single measurements at several analyte concentrations. Linearity correlation coefficient above 0.9993 is acceptable for most methods especially for major components in assay methods. The range of an analytical procedure is interval between the upper and lower concentration in the sample.

Precision

The precision of an analytical procedure expresses the closeness of agreement between a series of measurements obtained from multiple sampling of the same homogenous sample under prescribed conditions. Precision was determined by intra - day and inter –day study. The repeatability of the method was evaluated by carrying out the assay 3 times on the same day and intermediate precision was evaluated by carrying out the assay on 3consecutive days for the sample solution. The percent relative standard deviation (% RSD) was calculated.

Accuracy (Recovery studies)

Accuracy of an analytical procedure expresses the closeness of agreement between the value which is accepted either as conventional true value or on an accepted reference value and the value found.

Ruggedness

The method ruggedness is defined as the reproducibility of results when the method is performed under actual use condition. These include different analysts, laboratories, columns, instruments, source of reagents, chemicals, solvent and so on. The method ruggedness may not be known when a method is first developed, but insight 8is obtained during subsequent use of that method.

Robustness

The concept of robustness of an analytical procedure has been defined by the ICH as “a measure of its capacity to remain unaffected by small, but deliberate variations in method

parameters". The most important aspect of robustness is to develop methods that allow for expected variations in the separation parameters. For the determination of methods robustness, parameters such as variation in detector wavelength are varied with in a realistic range and the quantitative influence of the variables is determined.

LOD and LOQ

The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantified as an exact value. The quantification limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be quantitatively determined with suitable precision and accuracy. LOD AND LOQ were calculated using following formula LOD =3.3(SD)/S and LOQ =10(SD)/S, where SD= standard deviation of response (absorbance) and S= slope of the calibration. the results of LOD and LOQ are shown in table 2.

RESULTS AND DISCUSSION

For the selection of analytical wave length of mesalamine by appropriate dilutions of standard stock solution and scanned in the spectrum made from 200- 400nm thermo double beam UV spectrophotometer the λ max of 303 nm was selected for the determination of mesalamine and absorption maxima. The calibration curve for mesalamine was prepared in the concentration range 5-25 µg / ml. The proposed method obeys the Beer's law in the concentration range 5-25 µg / ml with good correlation coefficient (r^2= 0.9993). optical characteristics and data concerning to the method is represented in the **Table 2** .Recovery studies are done by addition of known amount of standard drug solution to pre analyzed tablet sample solution at three different concentration. Recovery in the range of 99.53 to 100.41. LOD and LOQ for the determination of mesalamine were 0.58219 µg / ml to 0.91836 µg / ml respectively.

Table – 1: Linearity data for mesalamine.

S.N0	Concentration	Absorbance
1	5	0.183
2	10	0.38
3	15	0.551
4	20	0.732
5	25	0.915

Linearity data for mesalamine

Table – 2: Optical Characteristics Of Mesalamine By Uv Method.

Parameters	Method
lmax (nm)	303
Beers law limit (mg/ml)	5-25
Sandell's sensitivity (mg/cm2/0.001 A.U)	0.03154
Molar absorptivity (L mol–1 cm–1)	1.67311 X 10^3
Correlation coefficient (r)	0.9993
Regression equation (y=mx+c)	Y=0.09097X+0.00515
Slope(m)	0.09097
Intercept(c)	0.00515
LOD (mg/ml)	0.58219
LOQ (mg/ml)	0.91836
Standard error of mean of Regression line	0.06257

OPTICAL CHARACTERISTICS OF MESALAMINE BY UV METHOD

Table-3: Repeatability for quantification of formulation – MESALAMINE by [wallace] UV Method.

S.No.	Interday*	Intraday*
1	97.58	98.54
2	96.32	97.26
3	98.18	99.51
4	100.24	98.72
5	99.39	100.09
6	98.65	97.38
Mean	98.39	98.58
SD	0.28424803	0.3579412
% RSD	0.5671272	0.4729315
SE	0.1748703	0.2019834

Repeatability for quantification of formulation – MESALAMINE by [wallace] UV Method

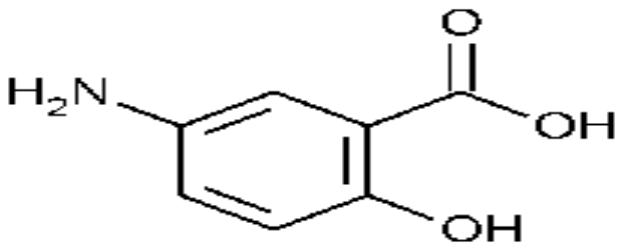
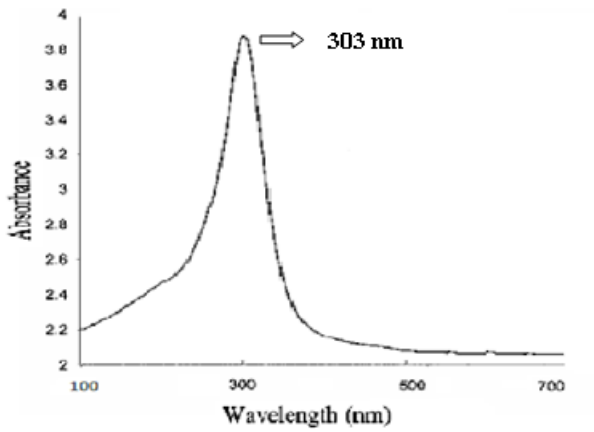


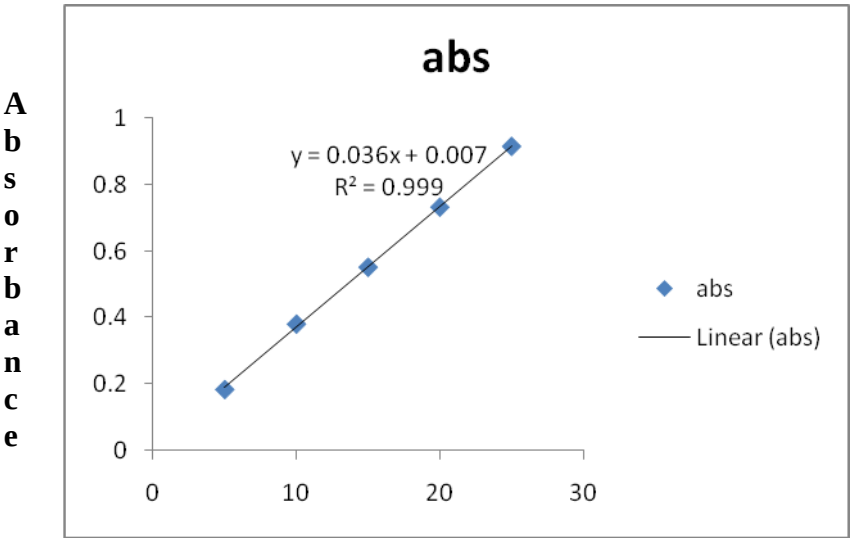
Figure: 1 Chemical Strucutre Of Measalamine.

CHEMICAL STRUCUTRE OF MEASALAMINE



UV spectrum of mesalamine in 1 N HCl

Figure- 2: UV spectrum of mesalamine in 1 N HCl.



Calibration curve of mesalamine by UV method

Figure 3: calibration curve of mesalamine by UV method.

CONCLUSION

The developed and validated UV spectrophotometer method was found to be cost effective due to the use of 1N HCL as a solvent throughout the experiment. None of the excipients employed in the formulation of mesalamine dosage forms. The plot is drawn between the concentration and absorbance which found to be linear in the concentration range of 5-25 µg / ml with good correlation coefficient greater than r^2= 0.9993. Low percentage relative standard deviation and highly precise and accurate thus the developed method for

mesalamine was found to be simple, precise, accurate, cost effective and it can be effectively suitable for routine sample analysis of mesalamine in commercial tablets.

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