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Development of UV spectroscopic technique for analysis of Meloxicam raw material and pharmaceutical dosage forms

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ABSTRACT

Meloxicam has been analyzed in a number of ways but the methods proved to be slow and tedious due to the involvement of buffers, maintaining of pH and lengthy process of HPLC or potentiometric titration. Our aim was development and validation of a new, fast, simple and inexpensive method for the analysis of Meloxicam by UV visible spectrophotometry. A new solvent system consisting of Acetonitrile and Methanol (70:30) was formulated by trial and error method. Different concentrations of meloxicam were made in this solvent system and were analyzed by UV visible spectroscopy. The absorbance was studied over the range of 240 to 400nm. The obtained results were used to study and calculate various validation parameters of this technique. The calibration curve was found to be linear over the range of 0.1 to 0.6ug/ml with linear coefficient of 0.999. The precision was calculated to be equivalent to 0.251%. The LOD and LOQ of this method were found to be around 0.006ug/ml and 0.02ug/ml respectively. The system showed accuracy over the range of 90-100%. This method proved to be a good alternative to existing reported methods as it showed sensitivity, accuracy as well as reproducibility with low cost and time.

Keywords: Meloxicam; UV spectrophotometry; Acetonitrile

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INTRODUCTION

Meloxicam is a non-steroidal anti-inflammatory drug (NSAID). Chemically, it is a derivative of oxicam and falls in the category of enolic group. It is a pale yellow fine powder, insoluble in water and acids.Meloxicam is used to relieve pain, fever, inflammation and swelling. It mainly acts by inhibiting cyclooxygenase, which acts in the production of prostaglandins. Hence, it is a widely used drug involved in the treatment of arthritis, pain, spondylitis etc.

This moiety has been discovered in 1996. Although much work has been done on it but a lot more aspects are yet to be discovered. Meloxicam has been evaluated by chromatography, electrophoresis, polarography, potententiometric, calorimetric and spectrofluorimetric methods. The newer and more advanced techniques of HPLC and UV spectrophotometry are now used for Meloxicam analysis.

Extensive research of Nageswara et al.[1] showed that UV and HPLC proved to be the most readily used method for analysis of drugs. This have been proved by reviewing a number of researches done on these techniques applied for analysis of meloxicam.[2,3,4,5,6,7,8,9,10,11,12,13,14,15]

Method validation is an important issue in drug analysis. The main aim of this study was to develop an easy, rapid and reproducible method for evaluation of validation parameters for Meloxicam analysis.

Most of the reported spectrophotometric and chromatographic techniques involve over two solvents[16,17,18,19,20,21,22]along with involvement of buffers[20,23,24,25,26]In case of buffer system, the formulation and maintenance of pH is very important as slight variation in pH may lead to faulty results. Secondly, the electrophoresis, colorimetric and HPLC methods have high cost of analysis in addition to be tedious and time consuming. Hence, our aim was to develop a much easier, simple and fast method with reduced cost and time of analysis.

MATERIAL AND METHOD:

Apparatus:

The spectrophotometric analysis was carried out on Schimadzu UV 2550 spectrophotometer. Bandelin sonoplus DT 2200 sonucator. Sartorius L420S analytical balance.

Chemicals:

Meloxicam working standard was donated by Pharmacare Laboratories Pvt Ltd. Acetonitrile, methanol, hexane, acetone, hydrochloric acid, sodium hydroxide, distilled water, acetic acid, gention violet, perchloric acid and sulphuric acid were of analytical grade, and purchased from Asif Chemicals Pvt Ltd. Pharmaceutical preparations of Meloxicam were purchased from local

pharmacy.In order to ensure purity of meloxicam, preliminary analysis of the drug using various methods such as melting point, loss on drying, residue on ignition and volumetric titration, was done.

Preparation of solvent system:

The solvent system was prepared by mixing carefully 70ml acetonitrile and 30ml methanol in volumetric flask.

Preparation of stock solution:

0.01gm of meloxicam was dissolved in 10ml of solvent system. 1ml of this solution was taken in volumetric flask and its volume was made up to 100ml with solvent. This makes up to 1mg/ml of stock solution of meloxicam.

Preparation of calibration standards:

0.2, 0.4, 0.6, 0.8 and 1ml of stock solution was taken by micropipette. These solutions were diluted to 10ml with solvent system to make 0.2ug/ml, 0.4ug/ml, 0.6ug/ml, 0.8ug/ml and 1ug/ml dilutions.

Preparation of Sample solution:

25 tablets were weighed and average weight was taken. Five tablets were crushed. Powdered drug of weight equivalent to average weight was taken and dissolved in 100ml solvent system. Sample solution of different concentrations was prepared from this dilution.(28)

Procedure:

Equal volume of solvent was taken in both coverts of UV spectrophotometer and zero error was adjusted. Different dilutions of standard solutions were taken one by one and their absorbances were measured at 355nm. The same procedure was repeated for sample dilutions. The obtained results were used to study and calculate mathematically(28), various validation parameters such as precision, linearity, accuracy, limit of detection, limit of quantification etc.

RESULTS AND DISCUSSION:

In this study, we developed a new method to study the purity and authenticity of meloxicam other than the method given in official pharmacopeia. The new method was developed, and later validated and authenticated by various analytical methods.

The official method for analysis of meloxicam is potentiometric titration which is a slow, tedious and complicated method. This method is more time consuming and difficult method due to the use of buffers and maintenance of pH. A slight change in the composition of titrant and titrate may lead to faulty results. Previously the non-aqueous titration method was also used for analysis of raw material as well as tablet dosage form. Although this method gave the results within official

limit but this method was found to be slow with involvement of the preparation of standard solution of perchloric acid and its standardization using non-aqueous medium. Therefore our aim was to look into fast and sensitive method for analysis of meloxicam raw material as well as its determination in solid dosage form.

Initially, the solubility of meloxicam in various solvents such as water, polyethylene glycol, 1N NaOH, 1N HCl, Methanol, ethanol, chloroform, hexane, acetonitrile, were studied visually and results are given in Table-1.

Table-: Solubility of meloxicam in different solvents

Solvents	Solubility
Water	Insoluble
Polyethylene glycol	Insoluble
0.1M NaOH	Soluble
0.1M HCl	Insoluble
Methanol	Soluble
Ethanol	Soluble
Chloroform	Freely soluble
Hexane	Insoluble
Acetonitrile	Freely soluble
Acetone	Soluble

By literature review[10,16,17,22,27] it has been found that acetonitrile is most commonly used in the study of Meloxicam in combination with different solvents. This was due to its good solubility and inert nature in the presence of Meloxicam. Thus different combinations of solvent were made with acetonitrile and absorbance of Meloxicam was studied. From the results, it was concluded that combination of methanol and acetonitrile in ratio of 30:70 with Meloxicam, gave very clear peak without reactivity. This also revealed that neither the drug Meloxicam nor the solvents react with each other that is why a smooth clear peak was obtained at 355nm

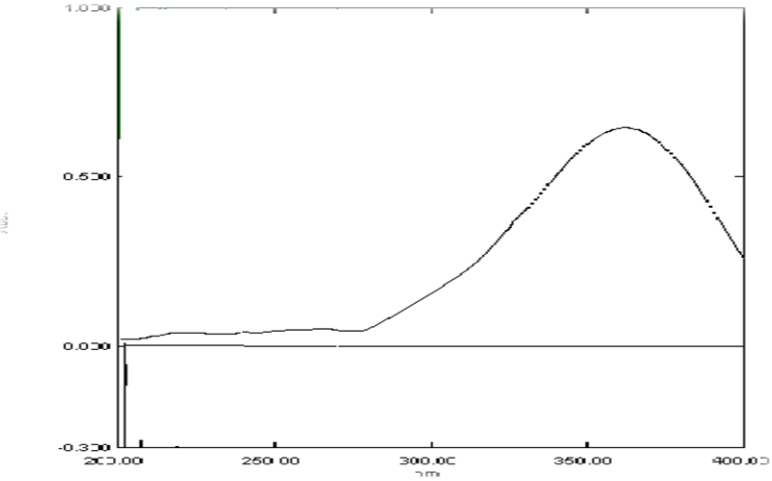

Figure 1: Sample peak of Meloxicam raw material obtained by UV spectroscopy.

Thus by trial and error method a good solvent system was developed to study the characteristics of Meloxicam. After the development of solvent system its application in different instrumental techniques for Meloxicam analysis were studied. The main instrument used in this research was UV visible spectroscopy. In UV visible spectroscopy, the solvent system used was acetonitrile and methanol (70:30).

Precision:

Precision of a method is the amount of closeness among individual test results when the procedure is applied repeatedly to multiple samplings. Precision is determined statistically by calculating standard deviation and relative standard deviation. (28) Table-2(a&b).

Table-2a: Precision of raw material by spectrophotometric method:

S.No	Concentration	Absorbance Nm	mean	Standard deviation	Relative standard deviation
1	1ug/ml	0.638	0.636	0.00160	0.251%
2	1ug/ml	0.638			
3	1ug/ml	0.634			
4	1ug/ml	0.638			
5	1ug/ml	0.637			
6	1ug/ml	0.636			

Result: At 355nm lambda max mean absorbance of six samples was found to be 0.636 with SD of 0.00160 and RSD 0.251%.

Table-2b: Precision of dosage form(Melfex tablet) by spectrophotometric method:

S.No	concentration	absorbance	mean	Standard deviation	RSD
1	1ug/ml	0.629	0.627	0.00167	0.266%
2	1ug/ml	0.628			
3	1ug/ml	0.628			
4	1ug/ml	0.628			
5	1ug/ml	0.624			
6	1ug/ml	0.626			

Result: At lambda max 355nm mean absorbance of six samples was found to be 0.627 with SD 0.00167 and RSD 0.266%

The precision was analyzed on both raw material and dosage form. This experimental work revealed that standard deviation and relative standard deviation of Meloxicam raw material were 0.0016 and 0.251%. Similarly the standard deviation and relative standard deviation of Meloxicam tablet was found to be 0.00167 and 0.266% respectively. This shows that the degree of resemblance among test results are very close and hence proved to be a good method in terms of repeatability and reproduction of results.

Linearity:

The amount of error that occurs when the readings change throughout an instruments measurement range is known as linearity (28). The linear response of the method was studied by measuring absorbance of different concentrations and plotting different concentrations from 0.1,0.2,0.3,0.4,0.5,0.6ug/ml verses their absorbance. The results obtained are given in the table3a & b, figure 2 and 3. A good determination coefficient 0.999 was obtained and calibration equation was found to be y=0.68x+0.002 for raw material and y=0.8329x+0.022 for dosage form.

Table-3a: Analysis of raw material of meloxicam by UV visible spectrophotometeric method:

S. No.	Concentration ug/ml	Absorbance nm
1	0.1	0.084
2	0.2	0.164
3	0.3	0.253
4	0.4	0.336
5	0.5	0.422
6	0.6	0.506

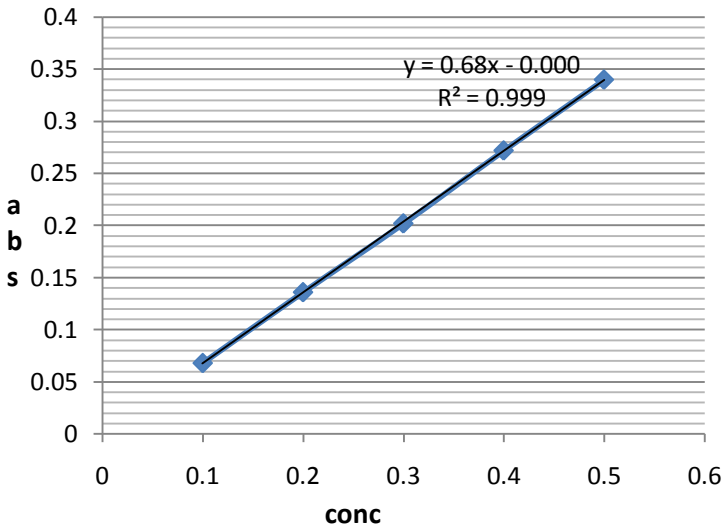

Figure 2: Calibration curve between concentration and absorbance of sample

Table-3b: Analysis of dosage form (Melfex tablet) of meloxicam by UV visible spectrophotometeric method:

S. No.	Concentration ug/ml	Absorbance nm
1	0.1	0.068
2	0.2	0.139
3	0.3	0.227
4	0.4	0.306
5	0.5	0.396
6	0.6	0.481

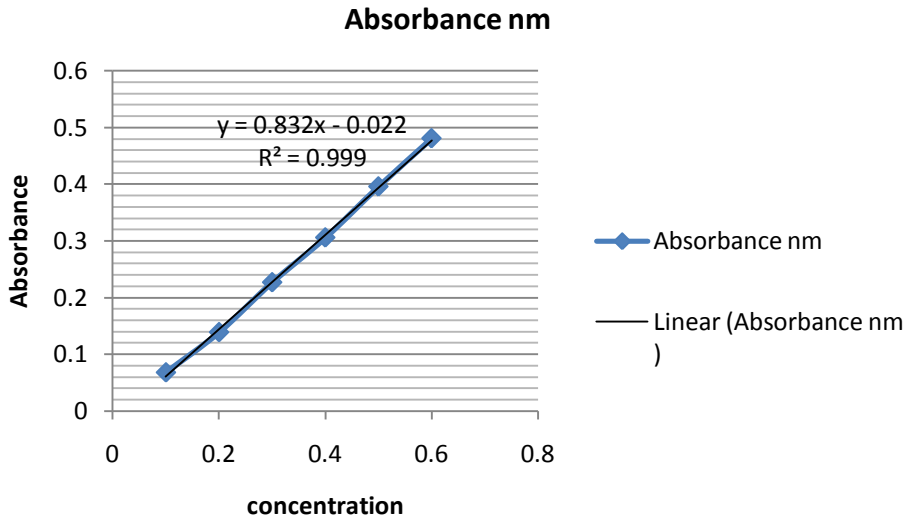

Figure-3: Calibration curve between concentration & absorbance of meloxicam dosage form

Sensitivity

Sensitivity refers to the lowest measurement of a given amount of sample that could be made by the analytical technique and is often denoted by two analytical factors, the limit of detection (LOD) and the limit of quantification (LOQ).The smallest concentration of the sample that can be detected is called as limit of detection (LOD) and limit of quantification is the determination of the smallest concentration of the sample (LOQ) with good precision & accuracy in the sample (28). The lowest concentration of sample that can be detected by this method was found to be 0.006ug/ml for raw material and 0.008ug/ml for tablet dosage form. This minute quantity shows that the system is capable of analyzing even very small amount of Meloxicam in the solution, table 4&5.

Table-4a: LOD and LOQ of Raw material:

S.no	Factor	Formula	Result
1	Limit of detection	3.3*SD/slope	0.006ug/ml
2	Limit of quantification	10*SD/slope	0.02ug/ml

Result: The LOD and LOQ are found to be 0.006ug/ml and 0.02ug/ml which is within the range.

Table 4b: LOD and LOQ of Tablet dosage form (melfax):

S. No.	Factor	Formula	Result
1	Limit of detection	3.3*SD/slope	0.008ug/ml
2	Limit of quantification	10*SD/slope	0.02ug/ml

Result: The LOD and LOQ are found to be 0.008ug/ml and 0.02ug/ml respectively.

*SD=standard deviation

Accuracy

Accuracy of a method is the degree of resemblance between an individual test result of the method

and the true value (28).

By applying this tool we determine the wavelength and its best accuracy while comparing with the standards. Calibration curves are constructed at all the wavelengths to check the accuracy of the spectrum.

Table-5: Determination of percentage purity of melfax tablet:

Sample no.	Absorbance of standard solution at 355nm	Absorbance of sample solution at 355nm	%purity=Sample ab/standard abs×100	%purity
1	0.631	0.629	0.629/0.631*100	99.6%
2	0.631	0.630	0.630/0.631*100	99.8%
3	0.633	0.631	0.631/0.633*100	99.6%
4	0.631	0.629	0.629/0,631*100	99.6%
5	0.630	0.629	0.629/0.630*100	99.8%
6	0.630	0.629	0.629/0.630*100	99.8%

Result: All %absorbance/percentage recovery are within limit.

CONCLUSION:

In this study, a simple and rapid UV spectrophotometric method, for the determination and analysis of Meloxicam in pharmaceutical formulation has been developed and validated.The linearity range, limit of detection and quantification, precision and accuracy were performed to determine the suitability of the method.This method has the advantage of being fast, simple, inexpensive and applicable over a wide concentration range with high precision and accuracy.These full validation assays has concluded that this newly presented UV method is linear, sensitive, accurate, precise and selective for the determination of meloxicam.The developed UV spectrophotometric method is cheaper, simpler and faster than other methods such as HPLC and potentiometery. These advantages encourage the application of this method in rapid routine analysis of meloxicam.

LIST OF SYMBOLS:

NSAID Nonsteroidal anti-inflammatory drug

HPLC High pressure liquid chromatography

UV ultra violet

LOD limit of detection

LOQ limit of quantification

BP British pharmacopeia

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