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DETERMINATION OF EVALUATION PARAMETERS OF ETODOLAC COMPARED WITH STANDARD BY USING UV-SPECTROPHOTOMETER

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ABSTRACT

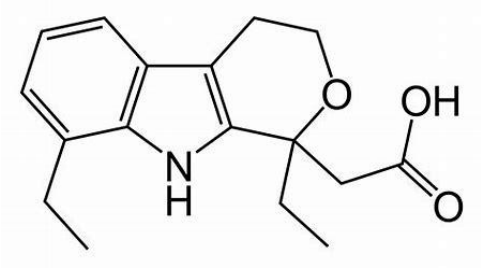
The present study deals with the comparison of validation parameters of marketed etodolac tablets (Etova 200mg) with API, by using UV spectroscopy. We are taken the absorbance ranges from 275-279.5 nm. Here we obey the Beer's lamberts law for the calibration of UV. Here we used methanol and water in 9:1 ratio for validation of marketed formulation and API, hence this method is very accurate and simple and less time consuming. This method was validated in terms of results of analysis were validated statistically and recovery studies. From the above study we concluded that there was higher linearity to the marketed formulation when compared with API. Other than this there is no much variation in other validation parameters.

KEYWORDS: Etodolac, UV, Linearity, Precision, Accuracy, Ruggedness, Robustness, LOD, LOQ, and Assay.

INTRODUCTION

Etodolac is a non-steroidal anti-inflammatory drug with analgesic, anti-inflammatory and antipyretic properties. Its therapeutic effects are due to its ability to inhibit prostaglandin synthesis. It is indicated to relief of signs and symptoms of rheumatoid arthritis and osteo arthritis. For acute and long-term management of signs and symptoms of osteo arthritis and rheumatoid arthritis, as well as for the management of pain. Etodolac is administered as a racemate. As with other NSAID, the S form has been shown to be active while the R form is

inactive. Both enantiomers are stable and there is no evidence of R to S conversation in in vivo. Similar to other NSAIDS, the S form has shown to be active while the R form is inactive. This decreases the synthesis peripheral prostaglandins involved in mediating inflammation. Etodolac binds to the upper portion of cox enzyme active site and prevents its substrate arachidonic acid from entering the active site. Etodolac was previously thought to be a non selective cox inhibitor, but it is now known to be 5-50 times more selective for cox-2 than cox-1. Antipyresis may occur by central action on the Hypothalamus, resulting in peripheral dilation, increased cutaneous blood flow, and subsequent heat loss.



MATERIALS AND METHODS

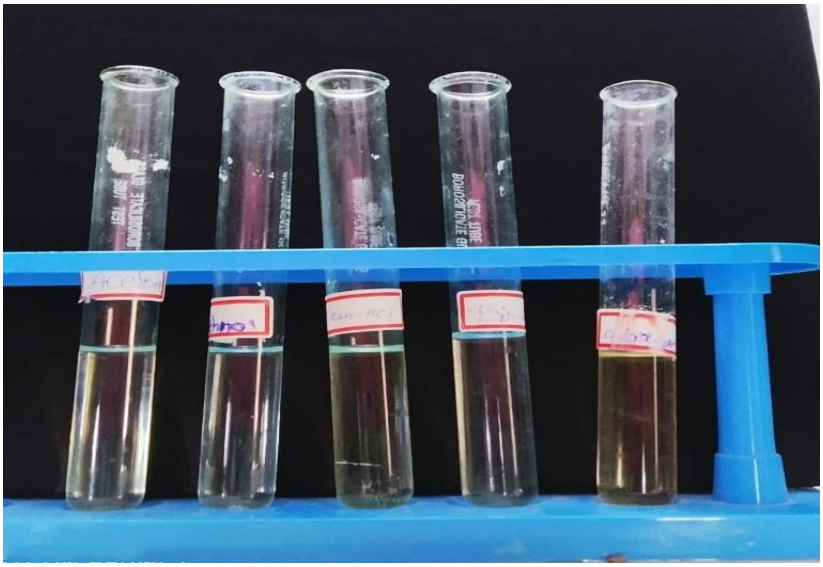
Sl.no	Solvents used
1.	Methanol
2.	Distilled Water
3.	Chloroform
4.	Concentrated Hydrochloric acid
5.	Acetone

The instrument used for the present study was GENESIS-10 UV-Visible spectrophotometer with Quartz cell size length 10mm, Diameter-45*12.5*12.5.

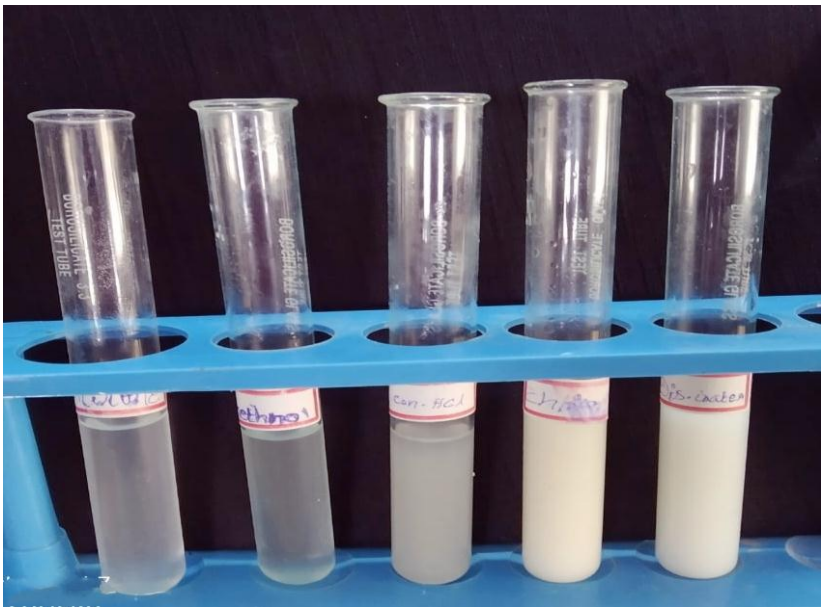
MATERIALS AND METHODS

Solubility

Solubility test for the drug Etodolac was performed by using various solvents. The solvents include distilled water, Methanol, Chloroform, Con.Hcl and Acetone. But it was found that Etodolac soluble in methanol and water in the ratio of 9:1.



Solubility for Etodolac Crude form.



Solubility for Etodolac Tablet form.

DETERMINATION OF λmax

Preparation of stock solution

The standard stock solution of Etodolac was prepared by transferring accurately weighed 30mg of drug to 50ml volumetric flask and dissolving it with water and methanol (1:9) to get a concentration of 3000µg/ml. The solution was diluted accordingly to a concentration of 300µg/ml and was kept as the stock solution. The prepared stock solution was diluted with water and methanol to get working standard solution of concentration 10-70µg/ml.

Preparation of sample stock solution

The standard stock solution of (30µg/ml) was scanned in the wavelength region of 275-279.5nm and the spectrum was recorded. Solvent methanol and water (9:1) was used as a blank. It was observed that λmax was found to be 275nm by plotting a graph between absorbance vs wavelength.

VALIDATION METHODS

Linearity

The standard stock solution of various dilutions in the concentration of 10µg/ml, 20µg/ml, 30µg/ml, 40µg/ml, 50µg/ml and 60µg/ml were prepared. The solution was scanned at 275-279.5nm and the absorbance was recorded.

Accuracy

The accuracy of proposed method was tested by recovery studies at 80%, 100%, 120% according to ICH guidelines by adding a known amount of pure drug to the pre-analyzed formulation concentration of 10µg/ml. The recovery results showed that the proposed method has an acceptable level of accuracy from 80-120µg/ml.

Preparation of standard stock solutions

Etodolac of 10mg was weighed and and transferred into 10ml volumetric flask, 5ml of the diluents was added and sonicated for 25min, further the volume was make up with diluent and filtered by Whatman filter paper (1000µg/ml of Etodolac).

Preparation of 80% spiked solution

8mg of Etodolac is weighed and transferred into 10ml volumetric flask, 5ml of solvent was added and sonicated for 25 min, further the volume was make up with solvent and filtered by whatman filter paper (80µg/ml of Etodolac). From this solution 0.1ml was taken into 10ml volumetric flask and make up to mark with solvent.

Preparation of 100% spiked solution

10mg of Etodolac is weighed and transferred into 10ml volumetric flask, 10ml of solvent was added and sonicated for 25 min, further the volume was made up with solvent and filtered by whatman filter paper (100µg/ml of Etodolac). From this solution 0.1ml was taken into 10ml volumetric flask and make up to mark with solvent.

Preparation of 120% spiked solution

12mg of Etodolac is weighed and transferred into 10ml volumetric flask, 10ml of solvent was added and sonicated for 25min, further the volume was made up with solvent and filtered by whatman filter paper (120µg/ml of Etodolac). From this solution 0.1ml was taken into 10ml volumetric flask and make up to mark with solvent.

Precision

Precision is the method verified by precision studies like, intra-day means analysis of the Etodolac respectively on the same day. Inter-day precision was checked by repeating analysis of Etodolac on a different day. Measurement of peak area for active compound was expressed in terms of %RSD for the compound for the method.

Preparation of sample stock solution

Weighed 10mg of Etodolac powder and transferred into 10ml volumetric flask 5ml of solvent were added and sonicated for 25min, further the volume was make up with solvent.

Intra-day precision

Three working sample solution of 10µg/ml, and the percentage amount and %RSD was calculated. As the limit of precision was less than "2" the system, then the precision was passed in this method.

Inter-day precision

Multiple sampling from a sample stock solution was done and three working sample solutions of 8µg/ml, 10µg/ml, 12µg/ml were prepared each injection from each working sample solution was given and obtained absorbance was mentioned in the table. Percentage relative standard deviation (%RSD) and were calculated for drug. As the limit of precision was less than "2", the system then precision was passed in this method.

Robustness

Robustness of the method was determined by carrying out the analysis under different temperature condition i.e. at 23℃, 25℃, and at 28℃ with different wavelength conditions that is at 275nm. The respective absorbances of 10µg/ml were noted and the result was indicated as %RSD.

Ruggedness

In ruggedness study, the influence of small, deliberate variations of the analytical parameters on the absorbance of the drug was examined. The factor selected was change in the analyst. The ruggedness of the method was determined by carrying out the analysis by different analyst and the respective absorbance of 10µg/ml was noted. The result was indicated as %RSD in the table.

Assay

Weigh accurately about twenty tablets and calculate the weights of individual tablets and finally calculate weights of individual tablets and finally calculate the average weights. They were triturated to fine powder by using a mortar and pestle. The powdered tablet equivalent to 25mg of Etodolac was dissolved in 15ml of methanol with help of sonication process and the final volume was make up to the mark with the methanol in 25ml volumetric flask. The resulted solution was filtered using whatman filter paper (0.45µg/ml). This final solution was further diluted to obtain 10µg/ml concentration of the solution by using methanol used as a solvent and observed by UV analysis.

RESULTS AND DISCUSSIONS

The method followed for validation of Etodolac was found to be precise ass the percentage standard deviation (%RSD) values for intra-day and inter day precision was found to be less than 2 better recoveries that is 0.6-0.7 for first order kinetics obtained at each added concentration indicating that the method was accurate. The LOD and LOQ were found to be with the limits indicating sensitivity of the method. The validated method was also found to be robust and rugged indicating the percentage recovery studies less than 2% that is respectively. Assay results indicated that the amount of drug was in good agreement with the label claim of respective formulation. The results were discussed in the following tables.

LINEARITY FOR CRUDE

S.no	Concentration (µg/ml)	Absorbance
1	10	0.251
2	20	0.335
3	30	0.458
4	40	0.584
5	50	0.713
6	60	0.815

LINEARITY FOR TABLET

S.no	Concentration (µg/ml)	Absorbance
1	10	0.061
2	20	0.187
3	30	0.346
4	40	0.458
5	50	0.601
6	60	0.751

Table 1: Accuracy Values For Crude Drug.

Level of Recovery	Sample Conc (µG/ML)	STD. Conc (µG/ML)	Total Conc. (µG/ML)	Amount Recovery	%Recovery	Mean Recovery	%RSD
80%	8	10	18	0.00799	99.87%	0.0021613	0.21607
100%	10	10	20	0.010827	100%	0.0020791	0.225110
120%	12	10	22	0.010	100%	0.0012764	0.109659

Table 2: Accuracy Values for Tablet Form.

Level of Recovery	Sample Conc (µG/ML)	Std Conc	Total Conc.	Amount Recovery	%Recovery	Mean Recovery	% RSD
80%	8	10	18	0.0079	98.87%	0.00357960	0.356
100%	10	10	20	0.0105	100%	0.00238327	0.251
120%	12	10	22	0.010	100%	0.00127644	0.109

PRECISSION

Intraday precision for crude Drug.

S.no	Concentration (µg/ml)	Absorbance	Statistical Analysis
1	10	0.473	MEAN=0.475 SD=0.0033787517 %RSD=0.71131
2	10	0.474	
3	10	0.476	
4	10	0.476	
5	10	0.479	
6	10	0.479	

Intraday precision for Tablet.

S.no	Concentration (µg/ml)	Absorbance	Statistical Analysis
1	10	0.627	MEAN=0.625 SD=0.00379598 %RSD=0.6063%
2	10	0.625	
3	10	0.624	
4	10	0.628	
5	10	0.625	
6	10	0.630	

INTER-DAY PRECISION

CRUDE

S.no	Concentration(µg/ml)	Absorbance	Statistical Analysis
1	80	0.391	MEAN=0.3913 SD=0.000472287581 %RSD=0.12062
2	80	0.392	
3	80	0.391	
4	100	0.729	MEAN=0.7286 SD=0.0004753945 %RSD=0.0625
5	100	0.728	
6	100	0.729	
7	120	0.824	MEAN=0.825 SD=0.001824828 %RSD=0.221
8	120	0.825	
9	120	0.826	

TABLET

S.NO	Concentration (µg/ml)	Absorbance	Statistical Analysis
1	80	0.365	MEAN=0.366 SD=0.001232882 %RSD=0.3363
2	80	0.368	
3	80	0.367	
4	100	0.468	MEAN=0.467 SD=0.00258009 %RSD=0.5524
5	100	0.467	
6	100	0.468	
7	120	0.781	MEAN=0.781 SD=0.000945145 %RSD=0.120924
8	120	0.783	
9	120	0.781	

RUGGEDNESS FOR CRUDE FORM

ANALYST-I

S.no	Concentration(µg/ml)	Absorbance	Statistical Analysis
1	10	0.626	MEAN=0.6295 SD=0.0048527 %RSD=0.770894
2	10	0.627	
3	10	0.629	
4	10	0.630	
5	10	0.632	
6	10	0.633	

ANALYST-II

S.no	Concentration (µg/ml)	Absorbance	Statistical Analysis
1	10	0.581	MEAN=0.584 SD=0.0040437606 %RSD=0.69242476
2	10	0.582	
3	10	0.583	
4	10	0.585	
5	10	0.586	
6	10	0.587	

ANALYST-III

S.no	Concentration (µg/ml)	Absorbance	Statistical Analysis
1	10	0.165	MEAN=0.1645 SD=0.0011107429 %RSD=0.67522364
2	10	0.166	
3	10	0.166	
4	10	0.162	
5	10	0.164	
6	10	0.167	

RUGGEDNESS FOR TABLET

ANALYST-I

S.no	Concentration (µg/ml)	Absorbance	Statistical Analysis
1	10	0.160	MEAN=0.1611 SD=0.001600 %RSD=0.99025
2	10	0.161	
3	10	0.161	
4	10	0.162	
5	10	0.162	
6	10	0.164	

ANALYST-II

S.no	Concentration (µg/ml)	Absorbance	Statistical Analysis
1	10	0.581	MEAN=0.582 SD=0.00451460 %RSD=0.775
2	10	0.582	
3	10	0.583	
4	10	0.584	
5	10	0.587	
6	10	0.580	

ANALYST-III

S.no	Concentration (µg/ml)	Absorbance	Statistical Analysis
1	10	0.580	MEAN=0.581 SD=0.00305068 %RSD=0.525
2	10	0.580	
3	10	0.581	
4	10	0.582	
5	10	0.583	
6	10	0.584	

ROBUSTNESS FOR CRUDE FORM

TABLE

AT 25℃

S.NO	Concentration (µG/ML)	Absorbance	Statistical Analysis
1	10	0.160	MEAN=0.1616 SD=0.001600 %RSD=0.99025
2	10	0.161	
3	10	0.161	
4	10	0.162	
5	10	0.162	
6	10	0.164	

AT 27℃

S.no	Concentration (µg/ml)	Absorbance	Statistical Analysis
1	10	0.581	MEAN=0.584 SD=0.00437606 %RSD=0.69242476
2	10	0.582	
3	10	0.583	
4	10	0.585	
5	10	0.586	
6	10	0.587	

AT 30℃

S.NO	Concentration (µG/ML)	Absorbance	Statistical Analysis
1	10	0.165	MEAN=0.1645 SD=0.0011107429 %RSD=0.67522364
2	10	0.166	
3	10	0.166	
4	10	0.162	
5	10	0.164	
6	10	0.164	

ROBUSTNESS FOR TABLET

TABLE

AT 27℃

S.NO	Concentration (µG/ML)	Absorbance	Statistical Analysis
1	10	0.626	MEAN=0.629 SD=0.0048527 %RSD=0.770894
2	10	0.627	
3	10	0.629	
4	10	0.630	
5	10	0.632	
6	10	0.633	

AT 29℃

S.NO	Concentration (µG/ML)	Absorbance	Statistical Analysis
1	10	0.581	MEAN=0.582 SD=0.00451460 %RSD=0.775
2	10	0.582	
3	10	0.583	
4	10	0.584	
5	10	0.587	
6	10	0.580	

AT 31℃

S.no	Concentration (µg/ml)	Absorbance	Statistical Analysis
1	10	0.580	MEAN=0.581 SD=0.00305068 %RSD=0.525
2	10	0.580	
3	10	0.581	
4	10	0.582	
5	10	0.583	
6	10	0.584	

DETERMINATION OF λ max FOR CRUDE DRUG

S.no	WAVELENGTH (nm)	ABSORBANCE
1	190	0.739
2	200	0.829
3	210	1.950
4	220	1.494
5	230	1.500
6	240	1.250
7	250	1.320
8	255	1.652
9	260	1.638
10	270	1.958
11	275	1.966
12	280	1.638
13	290	0.947
14	300	0.605

Table l: Determination of λMax For Tablet Form.

S.no	Wavelenth (nm)	Absorbance
1	190	0.212
2	200	0.565
3	210	0.489
4	220	0.464
5	230	0.563
6	240	0.723
7	250	0.497
8	255	0.644
9	260	0.872
10	270	1.277
11	275	1.323
12	280	1.316
13	290	0.916
14	300	0.173

Limit of Detection For Crude Drug

S.no	Wavelength	Absorbance	Statistical Analysis
1	275	0.092	MEAN=0.536 SD=0.0007332121 LOD=0.36
2	276	0.091	
3	277	0.090	
4	278	0.088	
5	279	0.088	
6	279.5	0.087	

Limit of Detection for Tablet.

S.NO	Wavelength	Absorbance	Statistical Analysis
1	275	0.086	MEAN=0.074 SD=0.002901 LOD=0.69
2	276	0.081	
3	277	0.075	
4	278	0.071	
5	279	0.068	
6	279.5	0.066	

Limit of Quantification for Crude Drug

S.NO	Wavelength (nm)	Absorbance	Statistical Analysis
1	275	0.039	MEAN=0.013 SD=0.0038374861 LOQ=0.284
2	276	0.021	
3	277	0.019	
4	278	0.013	
5	279	0.012	
6	279.5	0.012	

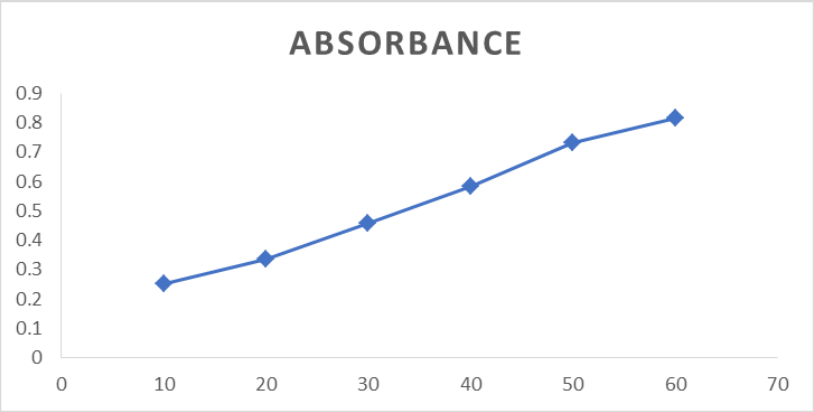
LIMIT OF QUANTIFICATION FOR TABLET

S.NO	Wavelength (nm)	Absorbance	Statistical Analysis
1	275	0.108	MEAN=0.097 SD=0.002691 LOQ=0.356
2	276	0.103	
3	277	0.097	
4	278	0.095	
5	279	0.091	
6	279.5	0.089	

Parameters and Their Ich Limits.

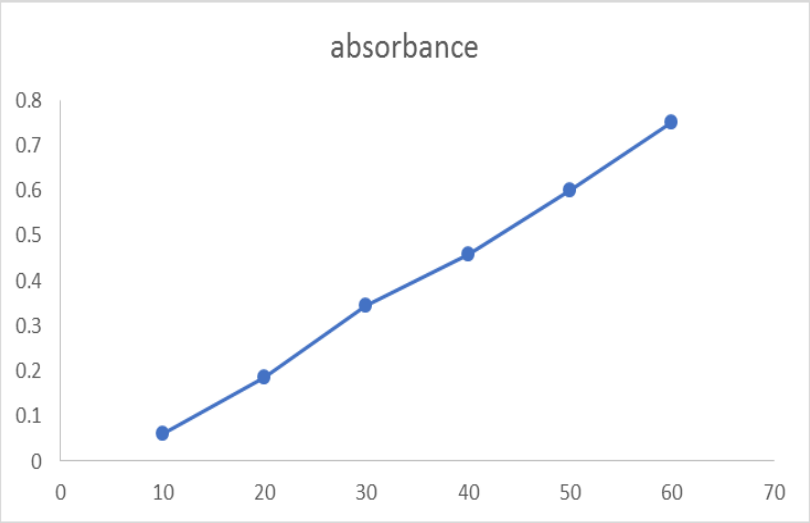
S.no	Parameters	Etodolac	Limits
1	Linearity	10-60µg/ml	R<2
2	Intraday precision for crude	0.711	R<2
3	Intraday precision for tablet	0.606	
4	Accuracy for crude	99.87%	98-102
5	Accuracy for tablet	99.87%	
6	LOD for crude	0.30	<3
7	LOD for tablet	0.69	
8	LOQ for crude	0.28	<10
9	LOQ for tablet	0.35	
10	Robustness for crude	0.785	R<2
11	R0bustness for tablet	0.690	
12	Ruggedness for crude	0.712	R<2
13	Ruggedness for tablet	0.763	
14	Assay for crude	100.00%	99=102%
15	Assay for tablet	99.9%	

Linearity for Crude



Concentration

Linearity for Tablet



Concentration

CONCLUSION

The bulk and dosage forms were validated in terms of Linearity, Specificity, Precision, Accuracy, LOD, LOQ, Robustness, Ruggedness and Assay. Results of the study were validated statistically and recovery studies. The validation results indicating that the linearity for the tablet shows more when compared to crude form of Etodolac. It was observed that there were no interference of impurities or excipients during the validation of drug formulation. This study thus exploits that the possibility for determining pharmacokinetic profile of Etodolac which may required in clinical study in near future. The proposed spectroscopic method was found to be simple, precise, highly accurate and less time consuming. Hence it is preferred method for analysis of Etodolac in bulk and dosage form.

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