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DISSOLUTION METHOD DEVELOPMENT AND VALIDATION FOR DERACOXIB CHEWABLE TABLET USING UV SPECTROPHOTOMETRIC METHOD

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Keywords:

Dissolution method development, validation, UV-Visible spectroscopy

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ABSTRACT: Deracoxib is a coxib class of Non Steroidal Anti-Inflammatory Drug (NSAID). Like other NSAIDs, its effects are caused by inhibition of Cyclooxygenase (COX) enzymes. Deracoxib causes greater inhibition of COX-2 than of COX-1. The aim of this proposed method was to develop and validate the UV spectrophotometric method for the routine quality control check of API containing 25 mg Deracoxib intablets dosage form. To investigate the most preferable dissolution method includes dissolution media as pH 6.8 sodium phosphate buffer + 1 % Sodium Lauryl Sulphate, 900ml, temperature as 37±0.5°C, RPM as 75, time 45 min. The absorbance maximum of Deracoxib was found to be 255nm. The concentration range of the proposed method was 5-15µg/ml and linearity as r^2 = 0.9959.The result of intraday &interday precision was 0.1458% and 0.1214% RSD respectively. The results of the percentage recoveries were 99.2%, 99.3%, and 99.1%. The effective dissolution method was developed and validated by UV spectrophotometer which used to be more applicable in various pharmaceutical industries.

INTRODUCTION: *In-vitro* drug dissolution testing is important parameters in pharmaceutical field used to check the releases of drug product in standard conditions. Deracoxib is a selective COX-2 inhibitor in dogs. Deracoxib is rapidly absorbed, with 90% bioavailability and peak plasma levels occurring 2 h following oral exposure in dogs [1]. Deracoxib is a coxib class of Non Steroidal Anti-Inflammatory Drug (NSAID). Like other NSAIDs, its effects are caused by inhibition of Cyclooxygenase (COX) enzymes. Deracoxib causes greater inhibition of COX-2 than of COX-1 [2]. The rate and extent at which the amount of drug substance is dissolved over a period of time is called dissolution.

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It is articulated as percentage release of drug substances present in dosage forms such as tablets, capsules, oral suspensions, transdermal patches, suppositories, semi preparations and ointments. It describes about manufacturing reproducibility, product performance similarity and biological availability of drug from its formulation [3]. Deracoxib is a Chemical group of Diaryl substituted pyrazole and Chemical name 4-[5-(3-difluro - 4 - methoxyphenyl) - (difluoromethyl) -1H pyrazole - 1 - y1 benzanesulfonamide. It has a molecular formula of $C_{17}H_{14}F_3N_3O_3S$ and molecular mass of 397.38 g/mol. Deracoxib is synthetic Nonsteroidal anti-inflammatory drug of the coxib class [4].

It has a role as a non-steroidal anti-inflammatory drug and a non-narcotic analgesic. It is a member of pyrazoles, an organ fluorine compound and a sulphonamide [5]. Extensive literature survey reveals that not a single analytical method has yet been reported for the dissolution of Deracoxib chewable tablets.

Our present study aims at first development of dissolution method for Deracoxib chewable tablets by UV-spectrophotometric method and validates the method as per ICH guidelines [6]. The dissolution procedure requires an apparatus, a dissolution medium, and test conditions that provide a method that is discriminating yet sufficiently rugged and reproduce able for day to day operation and capable of being transferred between laboratories [7].

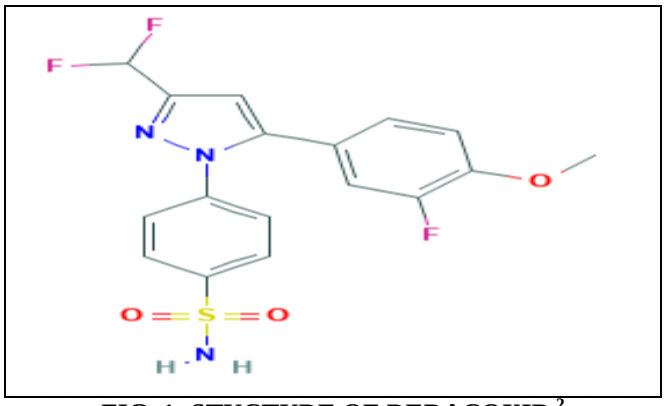

FIG. 1: STUCTURE OF DERACOXIB [2]

MATERIALS AND METHODS:

Instrument: A double beam UV-visible spectro-photometer (Shimadzu, model UV-1800) having two matched quartz cells with 1 cm light path and loaded with UV probe software (version 2.41) was used for recording of spectra and measuring absorbance. Dissolution studies were performed on USP Dissolution apparatus (Electrolab, Model: EDT-08LX). An electronic analytical weighing balance (0.1 mg sensitivity, Shimadzu AY 220), digital pH meter (DELUX model 101), a sonicator (sonica, model 2200 MH) were used in the study.

Chemicals and Reagents:

Reagents and Chemicals	Analytical Grade
Sodium dihydrogen phosphate monohydrate	AR Grade
Sulphate (SLS)	AR Grade
Sodium hydroxide	AR Grade
Acetonitrile	HPLC grade

EXPERIMENTAL WORK:

Dissolution Method conditions:

Dissolution Method Conditions: The optimized dissolution procedure includes the following by keeping the acceptance criteria for % drug release as not less than 80% (Q) of the labelled amount of deracoxib is dissolved in 45 min [7]. Dissolution media volumes were considered based solubility and on sink conditions [8].

Dissolution Medium: pH 6.8 Sodium Phosphate Buffer + 1% SLS
Dissolution Media Volume: 900 mL
Apparatus: USP Type II (Paddle)
RPM: 75
Sampling time Point (Q Point): 45 min
Sampling Volume: 10 mL
Temperature: 37 °C ± 0.5 °C
Working Concentration of Standard: 10 µg/mL
Working Concentration of Sample: 11.1 µg/ml
Detection Wavelength: 255 nm.

Preparation of Dissolution Media: pH 6.8 Sodium Phosphate Buffer + 1% SLS: Add 69 g of Sodium dihydrogen phosphate monohydrate into 10000 mL of demineralized Water. Mix Well. Adjust pH 6.8 ± 0.5 with dilute sodium hydroxide solution. Mix well; add 100.0 gm of SLS into it. Dissolve it.

Preparation of Standard Stock Solution: Transfer an accurately weighed quantity of about 50 mg of Deracoxib API into 50 mL volumetric flask. Add about 30 mL Acetonitrile, Sonicate to dissolve it, make volume up to mark with acetonitrile and Mix (1000 µg/mL).

Preparation of Standard Solution (for Strength: 25 mg / Tablet) Dilute 1 mL of stock solution into 100 mL with dissolution media. Mix well. (10 µg/mL).

Preparation of Sample Solution: Set the dissolution parameter of the instruments, as mentioned above. Place one tablet each in six different vessels, and operate the apparatus exactly for specified time. Withdraw about 15 mL of solution from a zone midway between the surface of the dissolution medium and top of the paddle, not less than 1 cm from the bowl wall. Filter the solution through Whatmaan filter paper, collect the filtrate. From filtrate withdraw 10 mL of the filtrate into 25 mL volumetric flask and make up the volume up to the mark with dissolution medium. (11.11 µg/mL)

Selection of λ_{Max}: Withdraw 1 mL from the standard stock solution into 100 mL volumetric flask and make up the volume up to the mark with dissolution medium (10 µg/mL). With this solution scan the spectra in the 200 – 400 nm UV range. Find out the λ_{max} from the graph.

100% target concentration for which UV spectrum was recorded. Suitable wavelength for the analysis was determined by recording UV spectrum in the range of 200-400 nm of for 10 µg/mL of deracoxib standard as above and λ_{max} was found to be 255nm and hence 255 nm was chosen for the analysis.

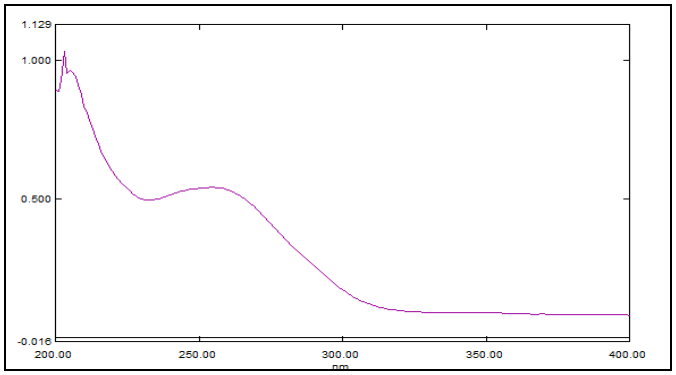

FIG. 2: UV SPECTRUM OF STANDARD (10 µg/ml)

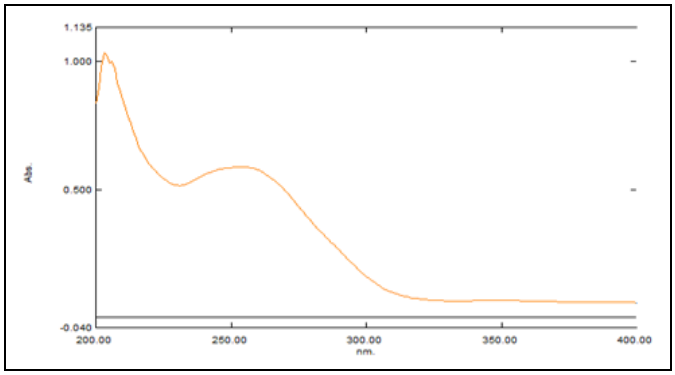

FIG. 3: UV SPECTRUM OF SAMPLE (11.11 µg /ml)

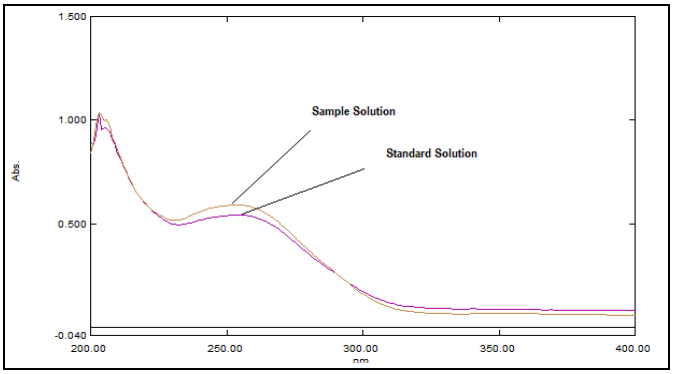

FIG. 4: OVERLAY UV SPECTRUM OF SAMPLE AND STANDARD

Method Validation: Validation of the analytical method is the process that establishes by laboratory studies in which the performance characteristics of the method meet the requirements for the intended analytical application. UV-spectrophotometric dissolution method developed was validated according to International Conference on Harmonization (ICH) guidelines. The method was validated for the parameters like specificity, linearity, accuracy, system precision, intra-day precision andinter-day precision / intermediate precision / ruggedness [7].

Precision:

System Precision: Six replicate recording of absorbance at 255 nm of standard solution at working concentration of 10 µg/mL showed % RSD (Relative Standard Deviation) less than 2, which indicates method, is system precise. System precision results are tabulated below **Table 1**.

Intraday Precision: Six replicate recording of absorbance at 255 nm of sample solution at working concentration of 11.11 µg/mL showed % RSD (Relative Standard Deviation) less than 2, which indicates method is precise. Intraday precision results are tabulated below **Table 2**.

Intermediate Precision (Inter day Precision / Ruggedness): Dissolution studies were performed on six tablets by different analysts on two consecutive days and % RSD of percentage drug release was calculated and was found to be less than 2, which indicate the method developed is inter day precise/rugged **Table 3**.

Linearity: Standard solutions of Deracoxib at different concentrations level (50%, 80%, 100%, 120% and 150%) were prepared. Linearity overlay curves were constructed for each concentration in the range of 200-400 nm UV visible range Fig 5. Calibration curve **Fig. 6** was constructed by plotting the concentration of drug versus absorbance at 255 nm.

The results show an excellent linear relationship between absorbance and concentration of drug within the concentration range of 5-15 µg/ml **Table**

4. The correlation coefficient was found to be 0.9959, which meet the method validation acceptance criteria and hence the method is said to be linear inthe range of 5-15 µg/ml.

Accuracy: Accuracy was determined by means of recovery experiments by the determination of % mean recovery of dissolution sample at three different levels 50, 100% and 150%. At each level, three determinations were performed. **Table 5** represents % mean recovery. Individual recovery and % mean recovery was found to be greater than 80% at 45 min, which indicates good recovery values and hence the accuracy of the developed method. **Table 6** summarizes the validation parameters about the developed dissolution method.

RESULT AND DISCUSSION:

Calculate % Drug Release by using following formula.

% Drug Release = AT / AS × WS / DS × DT / WT × P / 100 × Av. wt. / LC × 100

Where,

AT: Absorbance of analyte in sample solution.

AS: Absorbance of analyte in standard solution.

WS: Weight of API/working standard taken in mg.

WT: Weight of sample taken in mg

DS: Dilution of standard solution

DT: Dilution of sample solution

LC: Label claim (in mg)

P: Percentage purity of API/working standard on as is basis.

Linearity:

Method Validation: Precision:

System Precision:

TABLE 1: SYSTEM PRECISION RESULTS

N	Absorbance
1	0.540
2	0.542
3	0.541
4	0.540
5	0.543
6	0.542
Average	0.5413
STDEV	0.0012
% RSD	0.2235

Intraday Precision:

TABLE 2: INTRADAY PRECISION RESULTS

N	Absorbance	% Drug Release
1	0.549	91.15
2	0.548	90.98
3	0.550	91.31
4	0.549	91.15
5	0.548	90.98
6	0.549	91.15
Average	0.5488	91.12
STDEV	0.0008	0.1249
% RSD	0.1458	0.1371

Intermediate Precision (Inter day Precision/ Ruggedness)

TABLE 3: INTERMEDIATE PRECISION/ RUGGEDNESS RESULTS

N	% Drug Release	
	Day 1	Day 2
1	91.15	90.96
2	90.98	91.10
3	91.31	91.15
4	91.15	90.92
5	90.98	91.12
6	91.15	91.20
Average	91.12	91.07
STDEV	0.1249	0.1106
% RSD	0.1371	0.1214

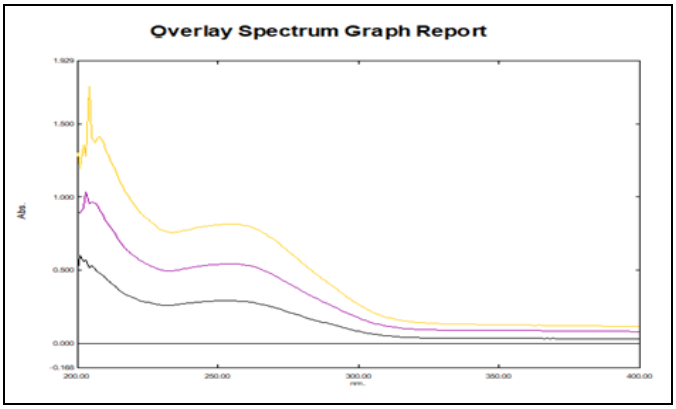

FIG. 5: LINEARITY OVERLAY SPECTRUM

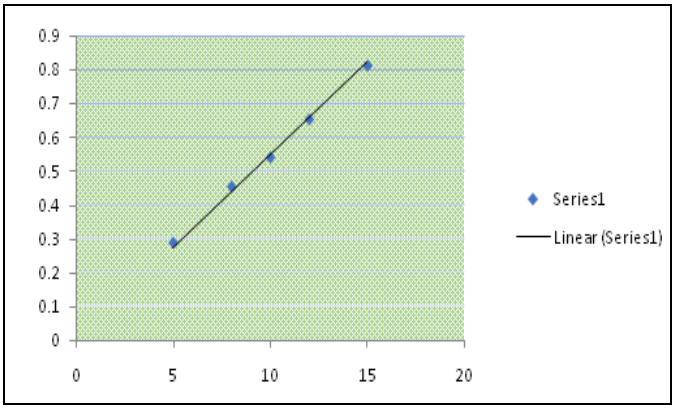

FIG. 6: CALIBRATION CURVE OF DERACOXIB

TABLE 4: CALIBRATION DATA FOR DERACOXIB

N	% Level	Concentration	Absorbance
1	50	5	0.289
2	80	8	0.455
3	100	10	0.541
4	120	12	0.654
5	150	15	0.813
r^2		0.9959	
Slop		0.0547	
Intercept		0.0301	

TABLE 5: RESULTS OF ACCURACY STUDIES FOR DERACOXIB

Concentration	Absorbance	% Recovery	% Mean Recovery
50%	0.284	98.3	99.2
	0.286	99.0	
	0.290	100.3	
100%	0.535	98.9	99.3
	0.540	99.8	
	0.537	99.3	
150%	0.802	98.6	99.1
	0.810	99.6	
	0.805	99.0	

TABLE 6: OPTICAL CHARACTERISTICS AND VALIDATION PARAMETERS OF DERACOXIB

Detection Wavelength (nm)	255 nm
Beer's Law limits (µg/ml)	5-15
Regression equation (y = mx+c)	y = 0.052x + 0.0301
Correlation coefficient	0.9989
Slope (m)	0.052
Intercept (c)	0.0301
(% RSD) System precision	0.2235
(% RSD) Intra-day precision	0.1371
(% RSD) Inter-day precision	0.1214
Accuracy (% Mean Recovery)	-
50 % Level	99.2
100 % Level	99.3
150 % Level	99.1

Specificity: Blank (pH 6.8 Sodium Phosphate Buffer) had zero absorbance at all wavelengths from 200-400 nm while standard solution exhibited UV spectrum, hence the method is said to be specific for the analyte of interest.

CONCLUSION: A simple dissolution method by UV-spectrophotometry method was developed and validated for the estimation of Deracoxib immediate release tablet as per ICH guidelines. The optimized method uses phosphate buffer pH 4.5 as a solvent and dissolution medium, and detection wavelength of 276 nm. The developed method resulted in Deracoxib exhibiting linearity in the range 1.25-5 µg/ml. System precision and intra-day precision are exemplified by relative standard deviation of 0.148% and 0.950% respectively. Method was found to be rugged as precision was found to be 0.924%. Accordingly it is concluded that the developed dissolution method by UV spectrophotometry is simple, accurate, precise, linear and rugged and therefore the method can be employed for the routine dissolution analysis of Deracoxib tablets in various pharmaceutical industries.

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CONFLICTS OF INTEREST: The authors confirm that this article content has no conflict of interest.

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