Stability Indicating Analytical Method for Simultaneous Estimation of Assay of Ibuprofen, Domiphen Bromide and Related Substances of Ibuprofen in Finished Formulation by UPLC

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ABSTRACT

To develop and validate a simple, fast, precise, selective and accurate UPLC method to determine the assay of Ibuprofen, Domiphen Bromide and Ibuprofen impurities in Ibuprofen suspension. Chromatographic separation has achieved on AQUITY UPLC BEH C18 column (2.1×100 mm), 1.7 µ particle size using mobile phase A as 0.1 % Ortho phosphoric acid and mobile phase B as 100 % Acetonitrile. The flow rate was 0.4 ml/min and detection wavelength carried out at 215 nm. The retention time of Ibuprofen, 4-Isobutyl acetophenone (Related Compound-C) and Domiphen Bromide was found 5.4 min, 6.5 min and 10.1 min respectively. The method has been developed and validated according to ICH guidelines. Ibuprofen, Domiphen Bromide and related impurities are completely separated with each other and with blank and placebo peaks. The linear range of Ibuprofen was 0.1 ppm to 750 ppm, Domiphen Bromide was 0.25 ppm to 3.75 ppm and 4-Isobutyl acetophenone was 0.24 ppm to 1.92 ppm. The recovery of Ibuprofen, Domiphen Bromide and 4-Isobutyl acetophenone were found in between 95.0 % to 105.0 %. The obtained cumulative % RSD of precision and intermediate precision study is 0.1 and 1.9 for Ibuprofen, 0.3 and 1.8 for Domiphen Bromide, 1.4 and 1.5 for 4-Isobutyl acetophenone. The developed method was precise, accurate and linear. It can be used for the testing for assay of Ibuprofen and Domiphen Bromide and Ibuprofen related substances in Ibuprofen suspension 100 mg/5 ml during routine quality control and stability testing.

Keywords: Ibuprofen, Domiphen Bromide, 4-Isobutyl acetophenone, RP-Ultra Performance Liquid chromatography (RP-UPLC), Validation, ICH Guidelines, Suspension.

INTRODUCTION

Ibuprofen is a non-steroidal analgesic, anti-inflammatory agent[1] and antipyretic. It has derived from propanoic acid by the research 193 arm of boots group during the 1960[2] and patented in 1961. Ibuprofen is available under a variety of popular trademarks, including nurofen, motrin, nuprin, advil. Originally marketed as brufen and it reduces inflammation, relieves pain and fever. It is equivalent to aspirin in its anti-inflammatory effects. Ibuprofen is primarily used for rheumatoid arthritis. It is also used for pericarditis and patent ductus arteriosus.

Ibuprofen is a 'core' medicine in the World health organization's model list of essential medicines necessary to meet the minimum medical needs of a basic health care system. Ibuprofen was available in market as different dosage forms, those are 100 mg/5 mL suspensions and 200 mg tablets.

The literature survey reveals that very few analytical methods has established for the estimation of Ibuprofen[3-13] and Ibuprofen related compounds[14-16] in dosage forms by different techniques like by UV spectroscopy and HPLC.

To the best of our knowledge, there is no reported UPLC method for estimation of Domiphen Bromide, Ibuprofen and Ibuprofen related substances in Ibuprofen finished dosage form in a single analytical method. Hence, developed a fast, selective and sensitive analytical method for the estimation of Ibuprofen, Domiphen Bromide and Ibuprofen related substances in 100 mg/5 mL suspension dosage form using the Ultra performance chromatographic method (Fig. 1 to Fig. 3).

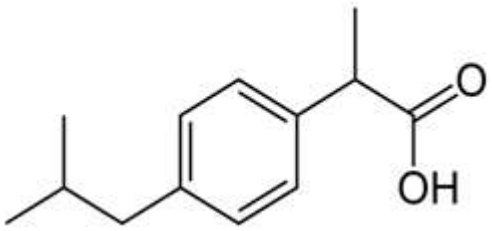

Fig. 1: Chemical structures of Ibuprofen

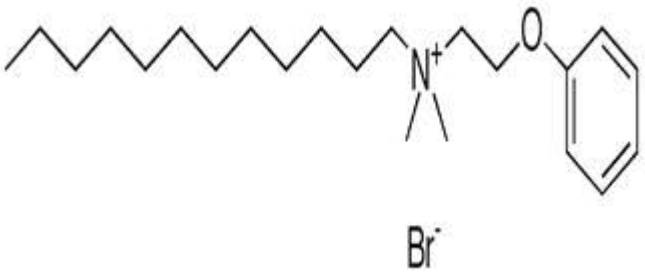

Fig. 2: Chemical structures of Domiphen bromide

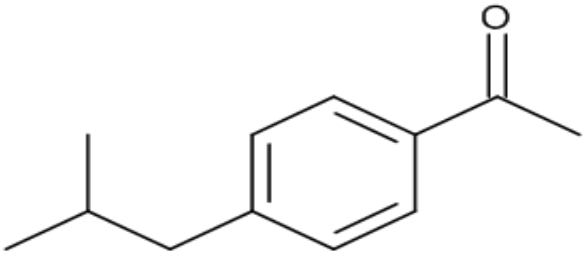

Fig. 3: Chemical structures of 4-Isobutyl acetophenone

MATERIALS AND METHODS

Ibuprofen, Domiphen Bromide and 4-Isobutyl acetophenone standards were a generous gift from a reputed pharmaceutical organization. Ibuprofen suspension, USP 100 mg/5 mL (Actavis, India) purchased from local markets. Acetonitrile was procured from Merck, India and Ortho-phosphoric acid were purchased from Loba Chemie, Mumbai, India. All used chemicals and solvents are analytical grade. Water used in the UPLC analysis was prepared by the water purifier (Arium®, 611UF, Sartorius, Germany). The mobile phase was filtered through a 0.45 µm membrane filter (Merck, Millipore) prior to use.

Preparation of solutions

Mobile phase preparation

Mobile phase A: Use 0.1 % ortho phosphoric acid
Mobile phase B: Use 100 % Acetonitrile

Diluent preparation

Mix 0.1 % ortho phosphoric acid and acetonitrile in the ratio of 50:50 % v/v.

Blank preparation

Transfer 10 mL of water to a 200 mL volumetric flask and dilute to volume with diluent and mix well.

Chromatographic conditions

Column	: AQUITY UPLC BEH C18 (2.1×100 mm), 1.7 µ from waters
Flow rate	: 0.4 mL/ min
Injection volume	: 3.0 µl
Column temperature	: 60° C
Sample temperature	: 25° C
Wavelength	: 215 nm
Run time	: 15 min
Elution Mode	: Gradient program (Table1)

Preparation of Domiphen Bromide stock solution

Weigh quantitatively and transfer 10 mg of Domiphen Bromide standard into 200 mL volumetric flask. Add 10 mL water to dissolve and make up to the volume with diluent.

Preparation of Ibuprofen standard solution

For assay of Ibuprofen, Domiphen Bromide and related substances of Ibuprofen:
Weigh quantitatively and transfer 50 mg of Ibuprofen working standard into a 100 mL volumetric flask. Add 10 mL of water and 60 mL of diluent and sonicate for 5 min to dissolve. Then add 5 mL of Domiphen Bromide stock solution and make up the volume up to mark with diluent and mix well.

Test preparation

For assay of preservative content, assay and related substances of Ibuprofen:

Place a clean and dry 200 mL volumetric flask on the pan of weighing balance. Transfer carefully 5 mL of sample into the volumetric flask. Add 10 mL of water and 60 mL of diluent. Shake well for 5 min for uniform mixing and sonicate for 30 min with intermediate shaking. Cool the solution to attain room temperature and dilute to volume with diluent and mix well. Filtered the solution through 0.45 µm nylon filter and inject into UPLC system.
Note: Sonication temperature should be maintained below 25°C.

Placebo preparation

Place a clean and dry 200 mL volumetric flask on the pan of weighing balance. Transfer carefully 5 mL of placebo into the volumetric flask. Add 10 mL of water and 60 mL of diluent. Shake well for 5 min for uniform mixing and sonicate for 30 min with intermediate shaking. Cool the solution to attain room temperature and dilute to volume with diluent and mix well. Filter the solution through 0.45 µm nylon filter and inject into UPLC system.

EXPERIMENTAL

Method optimization from HPLC to UPLC

Initially a HPLC method was developed by using C18, 4.6 X 250 mm, 5 µm with isocratic mode. Here the mobile phase was a mix of 0.1 % ortho phosphoric acid and 100 % Acetonitrile in the ratio 80:20 (% v/v) with 0.7 mL/ min flow rate, Column oven temperature at 40^{o}C and the detection was carried out at 215 nm with a run time of 60 min.

Later to decrease the run time a short UPLC method was developed by converting the above HPLC method to UPLC method.

Chromatographic conditions for UPLC method

AQUITY UPLC BEH C18 (2.1×100 mm, 1.7 µ) from waters with gradient program shown in table 1 about 0.1 % ortho phosphoric acid buffer as mobile phase-A and Acetonitrile as mobile phase-B at a flow rate of 0.4 mL/ min with the column oven temperature at 60^{o}C and the detection was carried out at 215 nm with a run time of 15 min. 4-Isobutyl acetophenone peak, Domiphen Bromide peak, Ibuprofen peak and its unknown impurities were well separated with each other.

After completion of method development, method validation was done as per USP and ICH guidelines.

Table 1: Gradient program

Time (min)	Flow (ml/min)	%A (0.1 % Ortho phosphoric acid)	%B (100 % Acetonitrile)
0.0	0.4	60	40
7.0	0.4	58	42
9.0	0.4	20	80
12.0	0.4	20	80
12.5	0.4	60	40
15.0	0.4	60	40

System suitability

System suitability was verified in accordance with USP general chapter <621> and evaluated the Tailing factor and % relative standard deviation for Ibuprofen and Domiphen Bromide in standard.

Specificity

The specificity was evaluated by injecting three blanks and three placebo solutions. The chromatograms were evaluated for any interference at the Ibuprofen, Domiphen Bromide and 4-Isobutyl acetophenone impurity.

Forced degradation studies

Forced degradation of Ibuprofen suspension carried out, to confirm that during stability study or throughout the shelf life, any degradation product if found will not interfere with the Ibuprofen, Domiphen Bromide and 4-Isobutyl acetophenone impurity. Also the forced degradation study will help to identify the type of degradation pathway (whether oxidative, alkali hydrolysis, acid

hydrolysis, photolytic, dry heat and humidity) for each of the degradants. In this study degraded the sample and calculated the mass balance.

Limit of detection and limit of quantification

The LOD and LOQ of the method are established by signal to noise ratio method, usually for LOQ 10:1, for LOD 3:1 can be quantitated and detected under the stated UPLC method.

Linearity

Linearity was conducted by preparing the eight levels of linearity solutions for Ibuprofen, Domiphen Bromide and 4-Isobutyl acetophenone (n=2) from 0.10 ppm, 0.30 ppm, 5.0 ppm, 50.0 ppm, 200.0 ppm, 500.0 ppm, 600.0 ppm, 750.0 ppm levels for Ibuprofen, 0.25 ppm, 0.50 ppm, 0.75 ppm, 1.00 ppm, 1.25 ppm, 2.50 ppm, 3.00 ppm, 3.75 ppm for Domiphen Bromide and 0.24 ppm, 0.48 ppm, 0.60 ppm, 0.84 ppm, 0.96 ppm, 1.248 ppm, 1.44 ppm, 1.92 ppm levels for 4-Isobutyl acetophenone. Based on the obtained data Draw linearity graphs for the peak area against concentration and calculated the correlation coefficient, y- intercept and slope.

Precision

Precision of method was evaluated by injecting six un spiked test sample preparations and six spiked test sample preparations **(**4-Isobutyl acetophenone spiked) from a homogenous sample of single batch, from the un spiked test samples estimated the % assay of Ibuprofen and Domiphen Bromide. From the Spiked test samples estimate the 4-Isobutyl acetophenone and calculated the % RSD for Ibuprofen, Domiphen Bromide and 4-Isobutyl acetophenone.

Accuracy

Accuracy study was executed to evaluate the recovery of the Ibuprofen, Domiphen Bromide and 4-Isobutyl acetophenone by spiking method. Recovery study was done by spiking Ibuprofen and Domiphen Bromide on placebo in the concentration of 50%, 100% and 150% level of test target concentration and spiking the 4-Isobutyl acetophenone in sample solution corresponding from LOQ to 150 % of specification level. The recovery samples were prepared in triplicate at each level and injected. % recovery of Ibuprofen, Domiphen Bromide and 4-Isobutyl acetophenone was calculated for all the levels.

Ruggedness

Ruggedness of method was evaluated by using different instrument, different day (other than the precision day) and different column by injecting six un spiked test sample preparations and six spiked test sample preparations **(**4-Isobutyl acetophenone spiked) from a homogenous sample of single batch, from the un spiked test samples estimated the % assay of Ibuprofen and Domiphen Bromide. From the Spiked test samples estimate the 4-Isobutyl acetophenone and calculated the cumulative % RSD for Ibuprofen, Domiphen Bromide and 4-Isobutyl acetophenone.

Range

Range of analytical method obtained from linearity, Precision and Accuracy data and this method is Linear, Accurate and Precise.

Robustness

Robustness of the method was assessed by varying the instrumental conditions such as flow rate (± 10 %) and column temperature (± 5°C). Robustness of the method was evaluated by system suitability and assay of formulation.

Solution stability

Solution stability was established for standard and sample preparations. Room temperature stability was established by injecting standard and sample at different intervals and calculated similarity factor for standard against fresh standard and % assay difference for test sample from initial assay.

Robustness

Robustness of the method were assessed by varying the instrumental conditions such as flow rate (± 0.01 ml), column temperature (± 2°C), mobile phase composition (0.09 % OPA and 1.11 % OPA) and wavelength (±2 nm). Injected the standard and samples (Triplicate preparations) in robustness conditions and compare the results with precision and calculated the cumulative % RSD for Ibuprofen and Domiphen Bromide.

RESULTS AND DISCUSSION

System suitability

The system suitability test was performed using six replicate injections of standard and evaluated the system suitability. The obtained results of % RSD for six replicates of Ibuprofen and Domiphen Bromide peak areas from standard were less than 2.0 % and the tailing factor was not more than 2.0 for Ibuprofen and Domiphen Bromide peaks in standard. System suitability parameters results presented in table 2.

Table 2: System suitability

S. No.	Active name	Tailing factor	% RSD of six replicates
1	Ibuprofen	1.1	0.2
2	Domiphen bromide	1.0	0.4

Specificity

Specificity study was performed and no interference was observed with the blank and placebo peaks and at the retention time of Ibuprofen, Domiphen Bromide (preservative) and Ibuprofen known impurities in Ibuprofen suspension. This shows that the excipients do not interfere with the Ibuprofen, Domiphen Bromide and 4-Isobutyl acetophenone impurity peak and also there is no interference with any known and unknown impurities (That were generated in forced degradation). The chromatograms for specificity parameter were shown in fig. 4 to fig. 12.

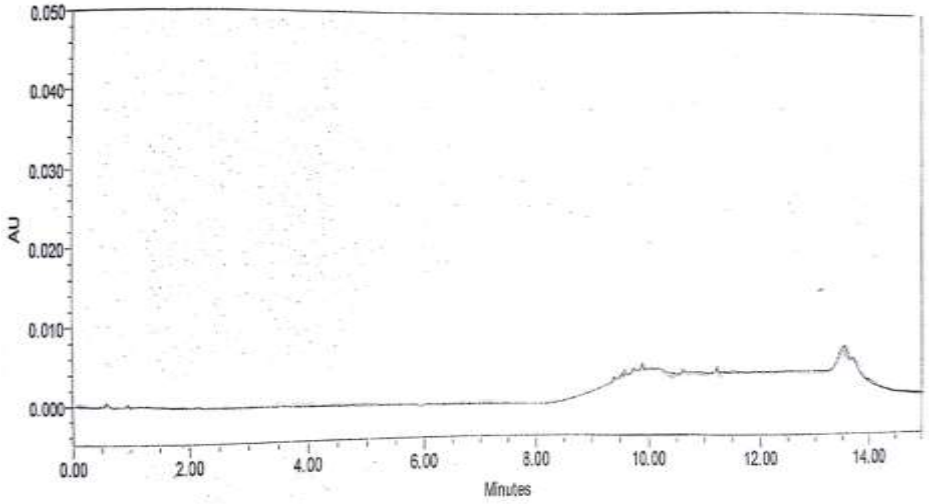

Fig. 4: Blank chromatogram

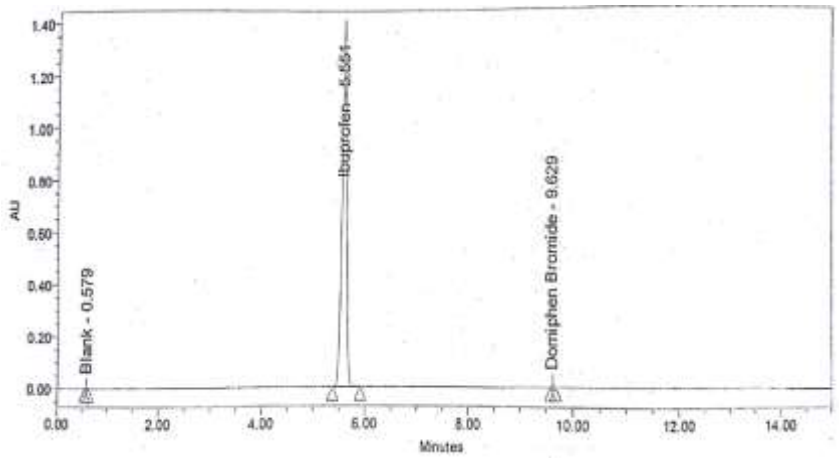

Fig. 5: Standard chromatogram

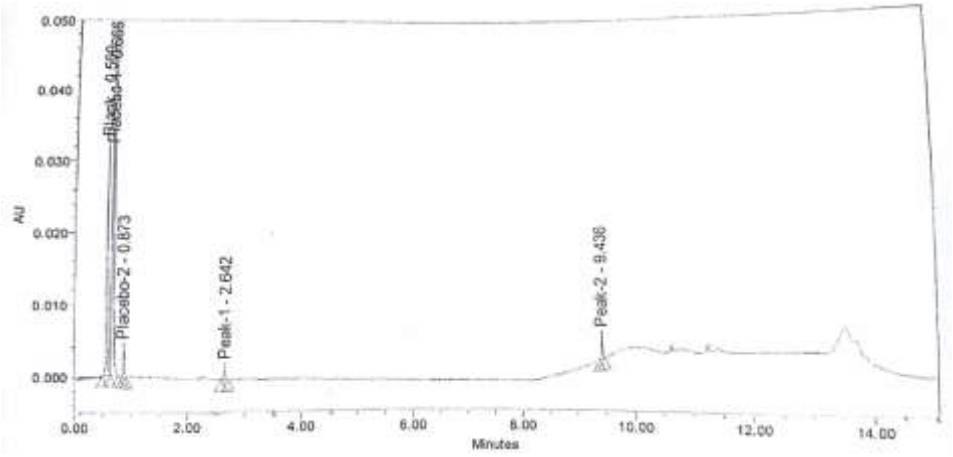

Fig. 6: Common Placebo chromatogram

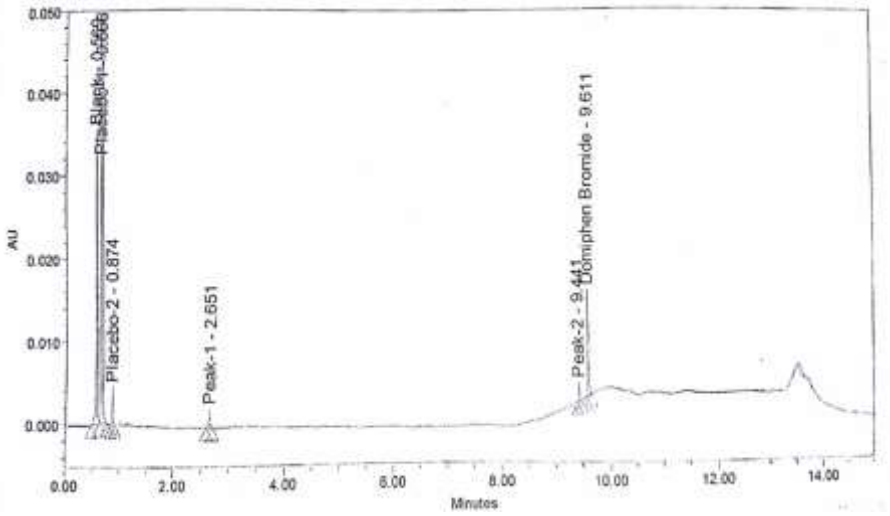

Fig. 7: Placebo with Domiphen Bromide chromatogram

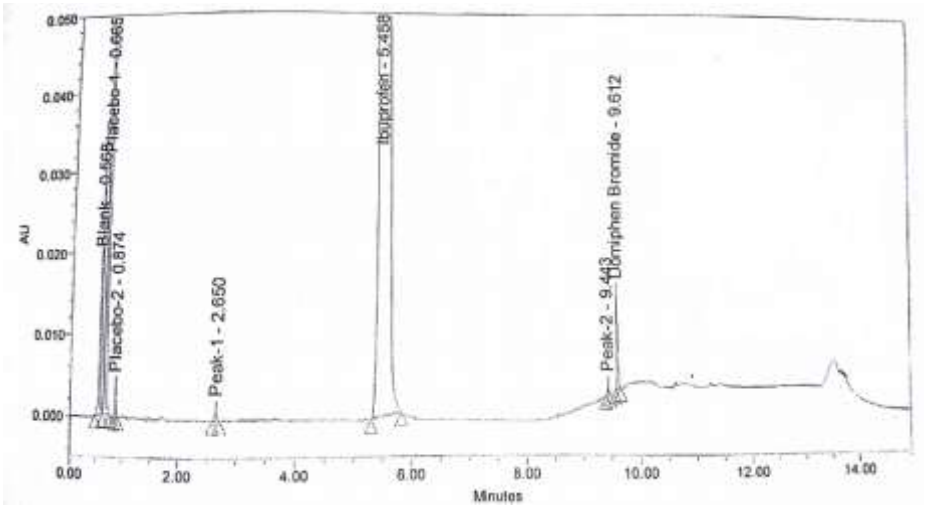

Fig. 8: As such sample chromatogram

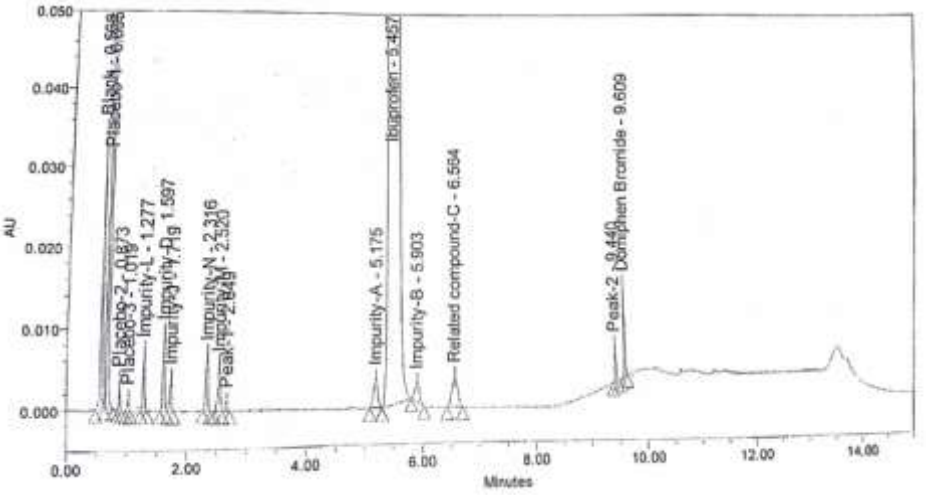

Fig. 9: Spiked sample chromatogram

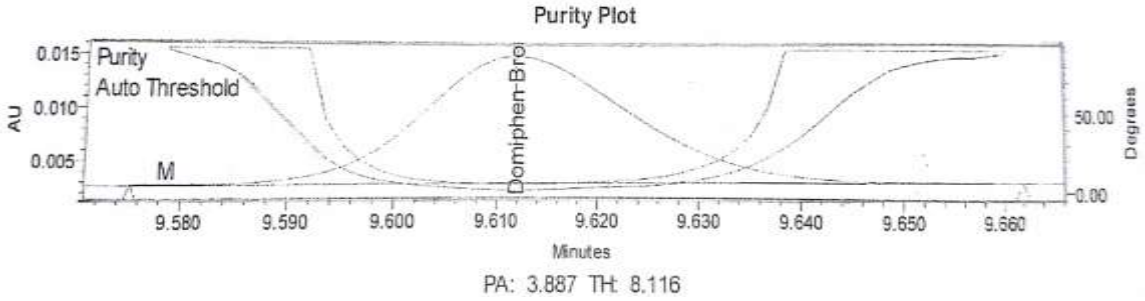

Fig. 10: Peak purity plot for Domiphen Bromide

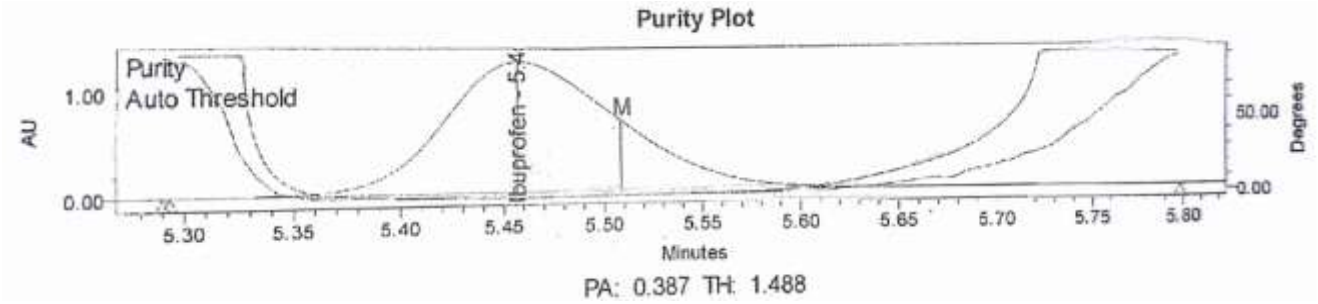

Fig. 11: Peak purity plot for Ibuprofen

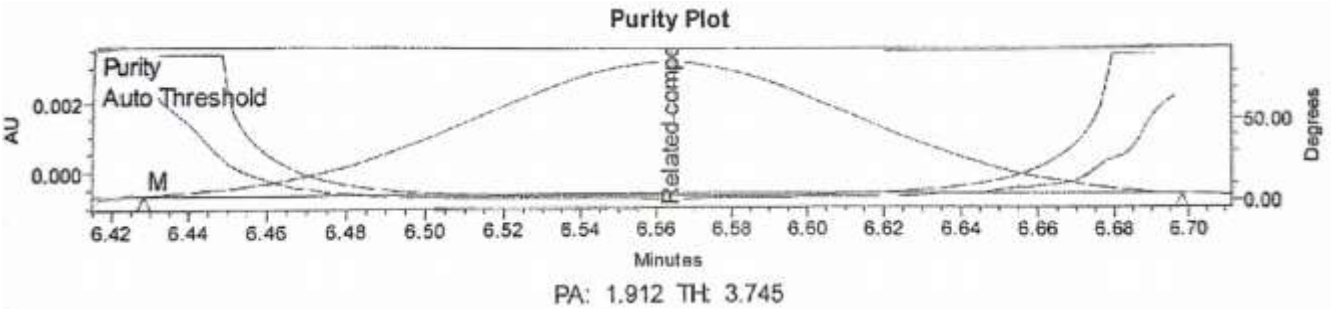

Fig. 12: Peak purity plot for 4-Isobutyl acetophenone

Forced degradation studies:

In force degradation studies, all generated impurities have not interfered with the Ibuprofen peak, Domiphen Bromide peak, 4-Isobutyl acetophenone impurity peak and also with each other. The purity angle of Ibuprofen and 4-Isobutyl acetophenone is less than the purity threshold. Forced degradation study's results are presented in table 3.

Forced degradation was attempted by using water, heat, light, acid, base, humidity and oxidizing agent. For acid degradation, the sample was treated with 2N hydrochloric acid (HCl) at 80°C for 2 h and then neutralized with 2N sodium hydroxide (NaOH). For alkali degradation, the sample was treated with 2N NaOH at 80°C for 4 h and then neutralized with 2N HCl. For oxidative degradation, the sample was treated with 0.001NKMNO_4 on the bench top for 30 min. For photolytic degradation, the sample was exposed to Ultraviolet (UV) (200 watt hour/m^2) as per ICH guidelines. For thermal degradation, sample was exposed to temperatures at 60°C for 2 d. For visible degradation study, the sample was exposed to 1.2 million Lux hours. For humidity degradation, the sample was exposed to 90 % RH at 25°C for 7 d.

After degradation treatments the samples were cooled to room temperature, diluted with the diluent, and injected for chromatographic analysis.

Blank, placebo and degradation impurities have not shown any interference with Ibuprofen peak, Domiphen Bromide peak, 4-Isobutyl acetophenone impurity peak, all unknown impurities and with each other. Hence it indicates that the method is stability indicating method.

Degradation condition	Ibuprofen		4-Isobutyl acetophenone		Total impurities (% w/w)	% Net Degradation	Mass Balance (%)
	Purity Angle	Purity Threshold	Purity Angle	Purity Threshold			
Unstressed sample	0.072	6.521	ND	ND	0.07	NA	NA
2N HCl /80°C For 2 h	0.937	18.154	0.156	0.875	6.67	6.77	102.5
2N NaOH /80°C For 4 h	0.616	22.332	ND	ND	0.06	0.06	101.8
VIS-NLT 1.2 Million lux hours	0.921	6.245	ND	ND	0.27	0.27	103.4
U.V Light at 254 nm for 168 h	0.412	8.939	ND	ND	0.06	0.06	100.5
Humidity 90 % RH at 25°C for 7d	0.454	6.808	ND	ND	0.08	0.08	101.5
0.001N KMNO4 for 30 min on Bench top	0.452	4.808	ND	ND	0.04	0.04	98.9
Thermal 60°C for 48 h	0.280	4.572	ND	ND	0.09	0.09	99.9

Limit of detection and limit of quantification

The LOD and LOQ are expressed as a known concentration of Ibuprofen and 4-Isobutyl acetophenone at a specified signal to noise ratio, usually for LOQ 10:1, for LOD 3:1 can be quantitated and detected under the stated UPLC method. The obtained results were at LOQ S/N for Ibuprofen was 10.5 at concentration 0.240 ppm, LOD S/N for Ibuprofen was 3.5 at concentration 0.079 ppm and LOQ S/N for 4-Isobutyl acetophenone was 10.8 at concentration 0.152 ppm, LOD S/N for 4-Isobutyl acetophenone was 3.1 at concentration 0.046 ppm respectively. The Chromatograms for LOQ & LOD level were shown in fig. 13 and fig. 14.

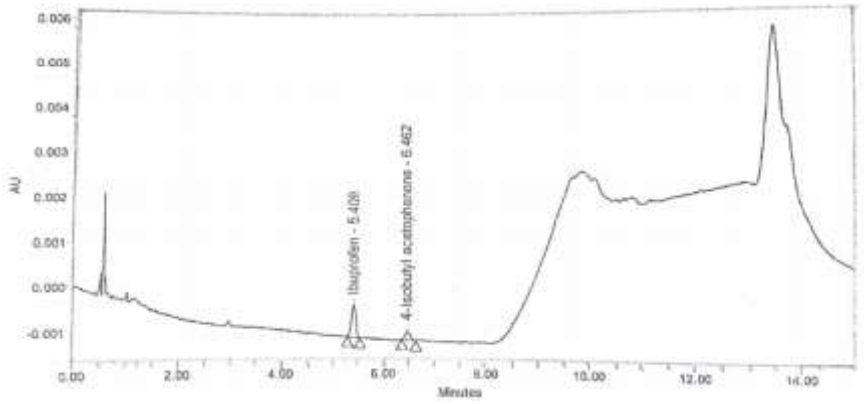

Fig. 13: LOQ Chromatogram

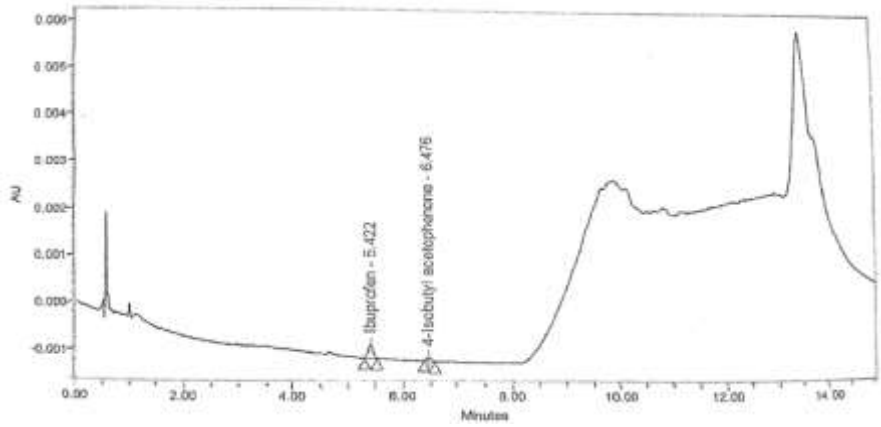

Fig. 14: LOD Chromatogram

Linearity:

Linearity was conducted by preparing the eight levels of linearity solutions for Ibuprofen, Domiphen Bromide and 4-Isobutyl acetophenone. Draw a linearity graphs for the peak area against concentration and linearity graphs shown in fig. 15, fig. 16 and fig. 17 for Ibuprofen, Domiphen Bromide and 4-Isobutyl acetophenone respectively. The graph was linear over the concentration range for Ibuprofen from 0.10 ppm to 750.0 ppm, Domiphen Bromide from 0.25 ppm to 3.75 ppm and 4-Isobutyl acetophenone from 0.24 ppm to1.92 ppm, and linearity data were presented in 4. Relative response factor (RRF) for 4-Isobutyl acetophenone impurity is 0.72 it is calculated from linearity data.

Table 4: Linearity of Ibuprofen, Domiphen bromide and 4-Isobutyl acetophenone

Linearity levels	Ibuprofen	Domiphen bromide	4-Isobutyl acetophenone
Correlation Coefficient (R)	1.000	1.000	1.000
Y-Intercept at	-2.20	-0.56	0.47
Slope	19548	9400	14151

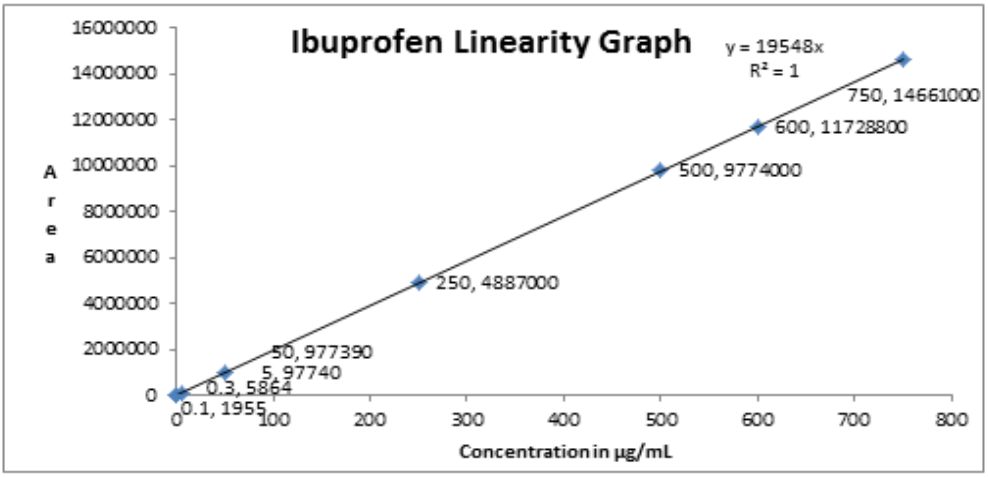

Fig. 15: Linearity graph for Ibuprofen

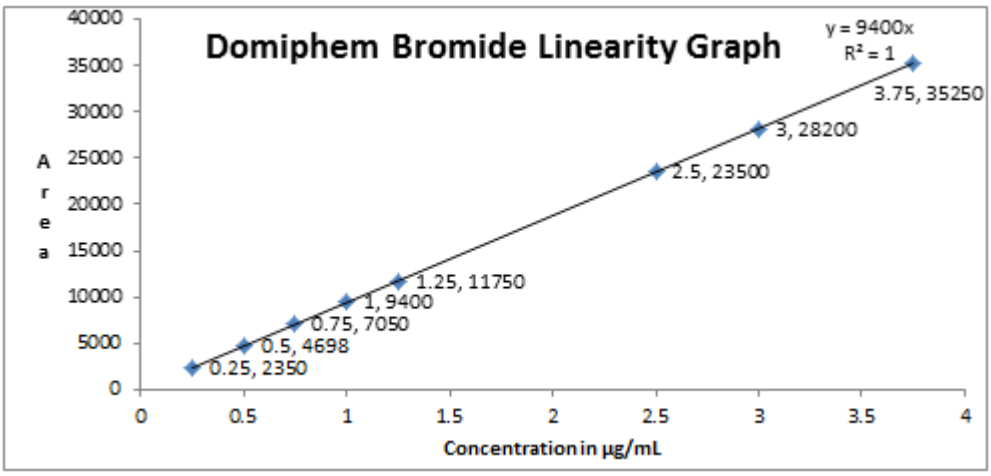

Fig. 16: Linearity graph for Domiphen bromide

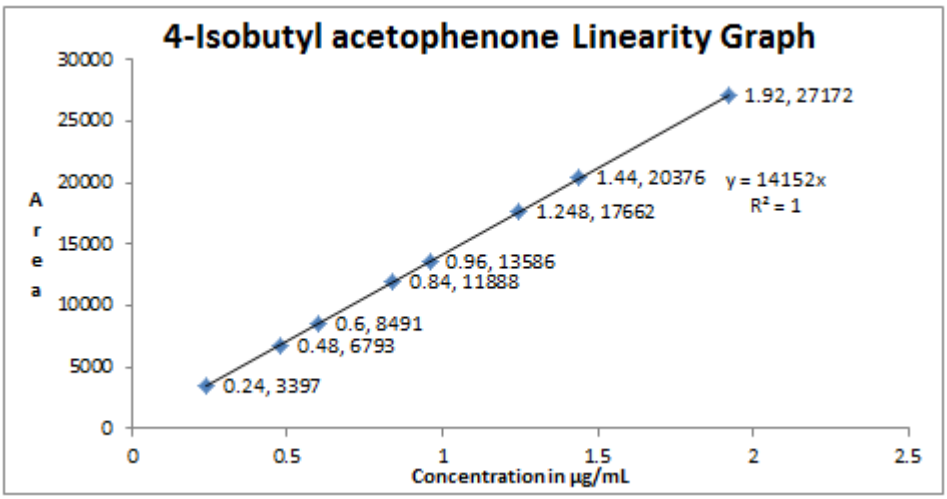

Fig. 17: Linearity graph for 4-Isobutyl acetophenone

Precision:

The result of Precision study was presented in table 5. % RSD values for Precision study is 0.5 for Ibuprofen, 0.3 for Domiphen Bromide, 1.4 for 4-Isobutyl acetophenone and the unknown impurities were not detected. The data demonstrated that the values have met the acceptance criteria. Hence the method is precise.

Table 5: Method precision for assay (%) of Ibuprofen, Domiphen Bromide and 4-Isobutyl acetophenone impurity (%w/w)

Sample No.	% Assay		Related substances (% w/w)
	Ibuprofen	Domiphen bromide	4-Isobutyl acetophenone
1	100.5	100.1	0.29
2	100.2	99.8	0.29
3	100.5	100.6	0.29
4	100.6	100.3	0.28
5	101.2	100.2	0.29
6	99.8	99.8	0.29
Mean	100.5	100.1	0.29
% RSD	0.5	0.3	1.4

Accuracy:

For Ibuprofen and Domiphen Bromide

The accuracy was performed by applying the method to a mixture of the excipients to which known amounts of Ibuprofen and Domiphen Bromide corresponding to LOQ (Only Ibuprofen), 50 %, 100 % and 150 % of label claim. Three test samples were prepared at each concentration and tested against a standard according to the description of the method. Each test solution was injected twice and all the found results were satisfactory and the results were presented in table 6.

For 4-Isobutyl acetophenone:

The accuracy was evaluated by spiking the 4-Isobutyl acetophenone in sample solution corresponding from LOQ to 150 % of specification level. Three spiked samples were prepared at each concentration and tested against a standard according to the description of the method. Each spiked sample solution was injected twice and all the found results were satisfactory and the results were presented in table 6.

This obtained recovery of the impurity proves that there was no interference from the excipients present in the formulation and the method is accurate.

Table 6: Accuracy of Ibuprofen, Domiphen bromide and 4-Isobutyl acetophenone (%Recovery)

Concentration level	% Recovery		
	Ibuprofen	**Domiphen bromide**	**4-Isobutyl acetophenone**
LOQ	98.8	Not performed	98.7
50%	100.6	99.4	100.6
100%	99.3	100.8	101.9
150%	100.8	100.6	100.3

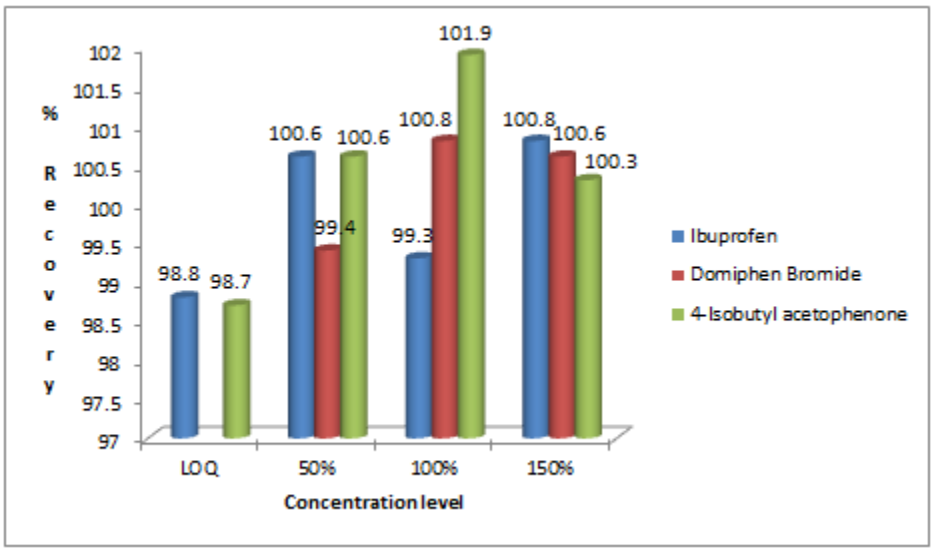

Fig. 18: Graphical representation data for Accuracy

Ruggedness (Intermediate precision)

The overall mean and overall %RSD results of precision and intermediate precision study were presented in table 7. % RSD values for Intermediate precision study are 0.2 for Ibuprofen, 0.5 for Domiphen Bromide, 1.5 for 4-Isobutyl acetophenone and the unknown impurities were not detected. The data demonstrated that the values have met the acceptance criteria. Hence the method is Rugged.

Table 7: Comparison between Method precision and Intermediate precision

Sample No.	**% Assay**		**Related substances (% w/w)**
	Ibuprofen	**Domiphen Bromide**	**4-Isobutyl acetophenone**
Mean for precision	100.5	100.1	0.29
% RSD for precision	0.5	0.3	1.4
Mean for Intermediate precision	100.2	99.9	0.28
% RSD for Intermediate precision	0.2	0.5	1.5
Overall mean (From 12 samples)	100.3	100.0	0.28

Overall % RSD (From 12 samples)	0.5	0.4	2.3

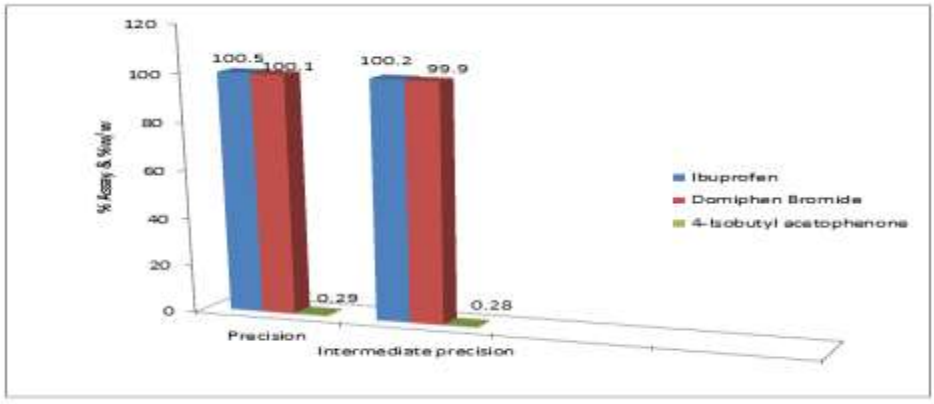

Fig. 19: Graphical representation data for Precision and Intermediate precision

Range

The range of this analytical method proved from 50% to 150% of target concentration for Ibuprofen and Domiphen Bromide and LOQ% to 150% of specification for 4-Isobutyl acetophenone.

Solution stability:

Stability of standard and samples:

The standard was found stable up to 48 h at laboratory temperature and sample was found stable up to 48 h at laboratory temperature with the absolute difference for % 4-Isobutyl acetophenone impurity, not more than ± 0.04 and total impurities not more than ± 0.1 from the initial value.

Robustness:

The deliberate changes in the method have no significant changes in retention time, relative retention time and no distorted chromatography were observed for Ibuprofen and Domiphen Bromide. This indicates that the method was robust. Results of robustness studies were presented in the table 8.

Table 8: Results of Robustness for Ibuprofen & Domiphen Bromide

Parameter	**Changes**	**Retention time (Minutes)**	**Ibuprofen**		**Retention time (Minutes)**	**Domiphen Bromide**	
		Ibuprofen	**% RSD**	**Tailing**	**Domiphen**	**% RSD**	**Tailing**

					Bromide		
Original method	N/A	5.48	0.1	1.2	9.63	0.6	1.2
Mobile phase composition	0.09 % OPA	5.73	0.1	1.3	9.91	0.2	1.2
	0.11 % OPA	5.35	0.1	1.3	9.52	0.4	1.2
Wavelength (±2nm)	213 nm	5.47	0.1	1.2	9.61	0.3	1.2
	217 nm	5.52	0.1	1.2	9.65	0.2	1.2
Flow Rate (±0.01 ml/min)	0.49 ml/min	5.72	0.2	1.2	10.12	0.4	1.2
	0.51 ml/min	5.23	0.0	1.2	9.24	0.5	1.1
Column oven temperature (±2^{o}C)	58^{o}C	5.73	0.0	1.2	9.77	0.3	1.2
	62^{o}C	5.38	0.1	1.2	9.54	0.1	1.1

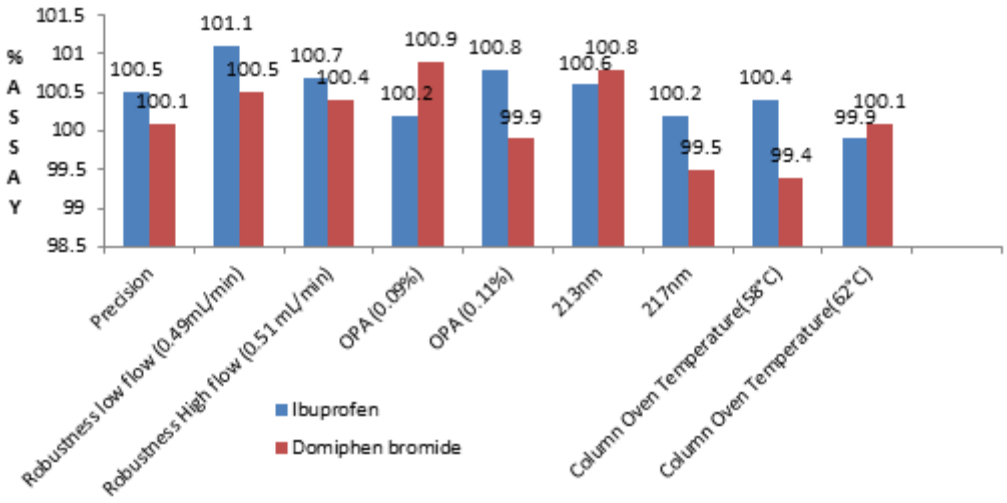

Fig. 20: Graphical representation data for Robustness study

CONCLUSION

A simple, rapid, accurate and precise stability indicating UPLC method by using Photo diode array detector for the analysis of Ibuprofen suspension in pure and in pharmaceutical dosage forms have been developed and validated in accordance with ICH guidelines. It is concluded that the Ibuprofen assay, Ibuprofen related substances and Domiphen Bromide (preservative) content method is validated and suitable for its intended purpose and it is suitable for the testing of in-vitro

assay, related substances and preservative content samples of Ibuprofen suspension 100 mg/ ml and tablets during routine quality control and stability testing.

The method have been satisfactorily applied to the simultaneous estimation of assay of Ibuprofen, Domiphen Bromide (preservative) content and Ibuprofen related substances of Ibuprofen in bulk and different formulation dosage forms like, Ibuprofen tablets 100 mg, 200 mg, 400 mg and 800 mg, Ibuprofen Oral solution 50 mg/1.25 ml, 100 mg/5 ml and 200 mg/5 ml.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

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