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DEVELOPED METHODS FOR DETERMINING IBUPROFEN CONTROLLED RELEASE MATRIX TABLETS USING RP-HPLC, HPTLC AND UV METHOD

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ABSTRACT
The current work details the creation of a new rapid, simple, sensitive, and reproducible RP-HPLC, HPTLC, UV Spectrophotometry method for the analysis of Ibuprofen. This approach has certain benefits in terms of its simplicity and sensitivity and is usable in routine analysis. An NSAID considered to be relatively safe is ibuprofen. Ibuprofen is available in several preparations at present. pharmaceutical dosage forms could be determined by a specific, linear, precise, accurate method as well as a system which was suitable for detecting carvedilol in bulk and pharmaceutical dosage forms.

Keywords: RP-HPLC, HPTLC, UV, Ibuprofen.

INTRODUCTION

Orally administered drugs dissolve in the stomach and permeate the epithelial membrane before being absorbed into the body. A major factor in the bioavailability of a drug is its dissolution rate, in addition to its solubility and permeability. Most drugs are concerned about their solubility in the gastro-intestinal system It is estimated that around 40% of the new drugs have poor solubility in aqueous solutions [1]. The result is a reduction in bioavailability and potential side effects Therefore, formulation scientists face the biggest challenge of solubilizing new drug substances, because of its ease of administration, high patient compliance, and flexibility in dosage form design, oral route has remained the most popular route for drug administration despite these challenges [2].

An NSAID considered to be relatively safe is ibuprofen. Ibuprofen is available in several preparations at present [3]. Among the world's most popular non-steroidal anti-inflammatory drugs, Ibuprofen has excellent analgesic, anti-inflammatory, and antipyretic effects. After a suitable dosage of Ibuprofen is administered, its pain-killing effect occurs almost immediately, while its anti-inflammatory effect takes a little longer Ibuprofen is alkyl benzene with a carboxylic acid functional group with pKa 2.48 and solubility of 21 mg L-1. Ibuprofen, its consumption is unlikely to be restricted since it is beneficial to humankind the non-steroidal anti-inflammatory drug (NSAID) [4].

Ibuprofen is widely used to treat gout and arthritis pain, tenderness, inflammation, and stiffness It is also used in the therapy of muscle ache, fever, menstrual pain and post-surgical pain the inhibition of COX-1 is responsible for unwanted effects on GI tract and platelet aggregation, whereas COX-2 is responsible for the analgesic, antipyretic, and anti-inflammatory activity of NSAIDs. However, the function of each isoform of COX on analgesic, antipyretic, anti-inflammatory activity, and the severity of gastric damage of NSAIDs is uncertain and different compounds can cause different degrees of physiological effects and gastric damage Ibuprofen considered a relative safe NSAID [5] NSAIDs have long been used in human medicine and have become accepted as relatively safe to the point where a number of NSAIDs are available over-the-counter without prescription. Currently, several ibuprofen preparations are available on the market. In the solid state, solid dispersions refer to one or more active ingredients dispersed in an inert carrier or matrix prepared either by comelting or solvent extraction or by a solvent-melt process Drug formulations using solid dispersions are excellent for improving the solubility of poorly water-soluble drugs, as well as for reducing the

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ulcerogenic properties of non-steroidal anti-inflammatory drugs [6]. Ibuprofen is a propionic acid derivative and belongs to non-steroidal anti-inflammatory drugs commonly known as (NSAIDS). Ibuprofen is used for various chronic inflammatory diseases like arthritis, primary dysmenorrhea and fever etc. Generally, Ibuprofen acts as vasodilator, causing dilation of coronary arteries and some other blood vessels. Ibuprofen is a core medicine in WHO's "Essential Drugs List" that serves as a list of minimum medical needs for a basic health care system [7].

RP-HPLC method for assaying Ibuprofen tablets
Method selection

The right chromatographic method should be chosen based on the drug's molecular weight, solubility, and nature. Due to the polar nature of ibuprofen, reverse phase chromatography has been applied.

Choosing a mobile phase

The injection of the drug ibuprofen with various mobile phases at various ratios and flow rates resulted in the acquisition of a sharp peak devoid of any interference peak containing spectrum. The various mobile phases contained acetonitrile, water, or tetrahydrofuran alone or in mixtures with two or three other solvents. Despite trying several ratios, no good results were produced.

Separation with acetonitrile and water

The separation was achieved using acetonitrile and water in different ratios. Despite this, it was discovered that the peak of ibuprofen was merging.

Separation with acetonitrile, tetrahydrofuran, and water

Various ratios of tetrahydrofuran, acetonitrile, and water were tried as mobile phases, but the peak shape was not satisfactory.

Acetonitrile and potassium dihydrogen phosphate buffer separation

In different ratios, potassium di hydrogen phosphate buffers and acetonitrile compositions were tested. It was possible to obtain symmetrical peaks with this method. For further study, we selected this mobile phase system since we sought good symmetrical peaks [8].

Method Optimization

Determined for Mobile phase ratio effects, Effect of flow rate, Selection of column, Selection of detector wavelength.

Assay By Hplc
Reagents used

Potassium di hydrogen phosphate, Formic acid, Acetonitrile, Water.

Preparation of Buffer Solution

Dissolve about 6.80g of potassium di hydrogen phosphate in1000 ml of HPLC/ Milli – Q water. Adjusts the pH to 3.0 ± 0.05 with formic acid.

Preparation Of Mobile Phase

Prepare a mixture of buffer and acetonitrile in the ratio of 60:40 Filter through 0.45µ Membrane filter and degas.

Standard Solution

Prepare the standard solution in duplicate calculate the similarity factor for standard-I and Standard - II solutions by using the following formula.

$$= \frac{\text{Area of standard solution} - 1 \; X \; \text{weight of STD (in mg) solution} - 2}{\text{Area of standard solution} - 2 \; (\text{1st injection}) \; X \; \text{weight of STD (in mg) solution} - 1}$$

Preparation Of Sample Solutions
For 25 mg tablets

Fill a 100ml volumetric flask with five tablets that have been weighed and transferred. Using a pipette, transfer 5ml of this solution into a 100ml volumetric flask and diluted up to the mark with mobile phase by adding 50ml of methanol and sonicating to dissolve. Pass the filtered water through a 0.45µ membrane filter.

Evaluation of system suitability
System suitability

Five replicate injections of the standard solutions were injected the percentage RSD for the peak area and tailing factor for ibuprofen were calculated.

Specificity

Blank, placebo, standard, sample solution injected into HPLC system. There was no interference from the blank and placebo at the retention time of ibuprofen peak. Peak purity reveals that ibuprofen peak was homogeneous and there were no co-eluting peaks at the retention time of ibuprofen peak [9].

Accuracy/Recovery

Known amount of ibuprofen spiked with placebo at about 80%,100%, and 120%of working concentration in triplicate and analysed as per testing procedure. The percentage recovery was calculated from the amount found and actual amount added.

Linearity And Range

The linearity of an analytical procedure is its ability (within a given range) to obtain test results which are directly proportional to the concentration (amount) of analyte in the sample. The range of the analytical

procedure is the interval between the upper and lower concentration (amount) of analyte in the sample (including the concentrations). For which it has been demonstrated that the analytical procedure has a suitable level of precision, accuracy, and linearity.

Preparation Of Standard Stock Solution

Weigh accurately and transfer about 62.52 mg of ibuprofen into a 100 ml volumetric flask. 50 ml methanol added and sonicated to dissolve, then make upto the volume with methanol. Pipette out 10 ml of this solution into a 100 ml volumetric flask and diluted upto the mark with mobile phase. Filtered through 0.45µ membrane filter [10].

Preparation Of Sample Solution

50 ml methanol added and sonicated to dissolve, then make up to the volume with methanol. Pipette out 10 ml of this solution into a 100 ml volumetric flask and diluted up to the mark with mobile phase. Filtered through 0.45 µ membrane filter. Inject 10µl of blank solution and each linearity level standard solutions into the chromatographic system and measure the peak area. The linearity of ibuprofen was performed in the range of 15.62µg/ml to 93.75µg/ml (25% - 150 % of working concentration). A graph was plotted with concentration in µg/ml on x axis and peak area on y axis. Slope, y intercept, correlation coefficient (r value), were determined.

Precision

Repeatability

Prepare the standard and sample solutions. Inject standard and sample preparations and record the chromatograms. Calculate the % content of ibuprofen.

Intermediate Precision (RUGGEDNESS)

Ruggedness of the method was verified by analysing the six samples of same batch which was used for method precision as per testing procedure. This study was performed by different analyst using different instrument and different column on different day. Calculated the percentage assay and percentage relative standard deviation for six assay results.

System Precision

Five replicate injections of standard solution were injected. The mean and percentage RSD for the peak areas of ibuprofen were calculated.

Method Prescision

Six samples of 25mg tablets were analysed as per test method. The percentage of assay and percentage RSD of six results were calculated.

Procedure

Injected all the standard and sample preparations and recorded the chromatograms. Calculated the % content of ibuprofen.

Solution Stability

By storing the sample compartment of HPLC instrument at ambient temperature, the stability of analytical solution was **verified** by analysing the standard and filtered sample solution initially and at different time intervals as detailed below. In the sample and standard solutions, we calculated the cumulative percentage RSD for peak areas of ibuprofen.

Hptlc Methods Developed And Validated For Estimation Of In Tablet Form

Selection of Mobile Phase

Several mobile phases were tested before one was selected by trial and error. A mobile phase was selected based on the Rf value of the drugs.

Fixed Mobile Phase

Ibuprofen, chloroform: methanol: toluene (1.5: 3: 3.5) was selected as mobile Phase.

Activation of Pre-Coated Plates

Activated by placing in oven at110-120ºc for 30 minutes after sample spotting

Sample Preparation

The standard stock solutions of 1000 µg/ml of ibuprofen were prepared by weighing 100mg of ibuprofen dissolved with methanol in 100 ml volumetric flask and made up to the volume.

Determined the Application of Sample, Spot Development, Photo-Documentation, Scanning, Spectrum scanning, Linearity.

Analysis Of Formulation

Preparation of Sample Solution

Twenty tablets were powdered and weighed equivalent to 100 mg of ibuprofen which is transferred in to a100ml volumetric flask and extracted with methanol the extract was filtered through Whatman filter paper No.41 and residue washed with methanol and made up to 100ml with methanol. Aliquot of 0.3µl solution of tablet formulation were applied and plate was developed with mobile phase.

Assay

The sample solutions were spotted along with the standard to check the specificity. From the peak area recorded the amount of the drug in the formulation was determined.

Method Validation

Method of Validation determined by Linearity, Accuracy and Precision.

Ibuprofen Quantification By Uv Spectroscopic Method

An UV method for estimating Ibuprofen is based on its chromophore system, which can absorb UV light.

Selection of Solvents, Selection of Wavelength

To prepare the stock solution, 100 mg of ibuprofen was dissolved in 100ml of methanol to obtain a concentration of 1000µg/ml. Methanol was used to dilute the stock solution, so that it contained 10µg/ml of ibuprofen. The UV absorbance of ibuprofen was scanned in this solution and the maximum absorbance was found at 242 nm. Therefore, 242 nm has been selected for the proposed study.

Preparation Of Standard Curve

Adequate dilutions were made from stock solution to get a concentration ranging from 1- 5µg/ml for ibuprofen using methanol. Absorbance of these solutions were measured at 242nm.

Quantification Of Ibuprofen In Formulation

The concentration of drug was determined by single point standardization method [11].

C test = A test× C std/ A std

RESULTS

RP-HPLC method for assaying Ibuprofen tablets

Specificity

There was no interference from the blank and placebo at the retention time of Ibuprofen peak. Peak purity reveals that ibuprofen peak was homogeneous and there were no co-eluting peaks at the retention time of ibuprofen peak.

The analytical method meets the acceptance criteria for accuracy study. Hence the method is accurate for the determination of assay of ibuprofen tablets.

Linearity And Range

Percentage relative standard deviation value indicates an acceptable level of ruggedness of the analytical method for the determination of assay of Ibuprofen tablets

Percentage RSD values indicates an acceptable level of precision of the analytical method for the assay of ibuprofen tablets.

Method Precision

Acceptance criteria

The percentage RSD for percentage assay from six samples is not more than 2.0.

Solution Stability

Acceptance criteria

The cumulative percentage RSD for peak area is not more than 2.0

LINEARITY

The linearity of the drug was determined by calibration curves and the linearity based on the area observed for ibuprofen. The regression co-efficient value for ibuprofen is 0.9989 respectively.

Method Validation

Linearity

Graphs of drug concentration versus peak area were plotted for each level of concentration and shown in the following diagram, Calibration parameters.

Precision

The intra-day coefficient of variation (%RSD) ranges between 0.12 and .43, and the inter-day coefficient of variation (%RSD) ranges between 0.34 and 0.51.

Table 1: Injection sequence

S.NO	DESCRIPTION	NUMBER OF INJECTION
1	**Blank**	**1**
2	**Std solution-1**	**1**
3	**Std solution- II**	**1**
4	**Std solution- II**	**4**
5	**Sample solution**	**2**
6	**Std solution**	**1**

Table 2: Robustness

PARAMETERS	NORMAL CONDTION	HIGHER SIDE	LOWER SIDE
pH	3	3.2	2.8
Flow rate	1.0ml per min	1.2 ml per min	0.8 ml per min
Wavelength	242nm	244 nm	240 nm

Table 3: HPLC study of Ibuprofen

Drug name	Retention time	Area	Theoretical Plate	Tailing factor
Ibuprofen	**2.95**	**4122906**	**5345.1**	**`1.38**

Table 4: System suitability of Ibuprofen

No of Injection	Area	Tailing Factor
1	4121145	1.51
2	4111958	1.53
3	4112954	1.54
4	4135075	1.51
5	4118578	1.56
Average	4119941	1.53
SD	9285.76	
%RSD	0.24	

Table 5: Accuracy

LEVEL	Amount found in µg	Actual Amount added in µg	%recovery	Mean	%RSD
Level-1 80%	**18.70 18.70 18.68**	**18.62 18.62 18.62**	**99.4 99.4 99.3**	**99.4**	**0.07**
Level-2 100%	**22.61 22.59 22.60**	**23.54 23.54 23.54**	**99.3 99.2 99.2**	**99.2**	**0.07**
Level-3 120%	**28.66 28.67 28.71**	**28.48 28.48 28.48**	**99.6 99.6 99.8**	**100.7**	**0.12**

Table 6: Repeatability of Ibuprofen

SAMPLE	Wt (mg)	AREA	% ASSAY
1	1698.25	4123817	96.51
2	1712.02	4117637	95.62
3	1725.02	4174680	96.26
4	1720.13	4152350	96.00
5	1735.14	4175361	95.74
6	1741.13	4193582	95.85
		Average	95.99
		SD	0.33
		% RSD	0.34

Table 7: Ruggedness of Ibuprofen

Sample No	Percentage of assay(w/w)	
	Analyst- I	**Analyst- II**
1	**98.4**	**98.0**
2	**98.9**	**96.0**
3	**99.5**	**96.4**
4	**98.6**	**96.1**
5	**98.4**	**97.9**
6	**99.6**	**97.7**
Average	**98.8**	**97.0**
%RSD	**0.51**	**0.98**

Table 8: Precision

S. No	Peak areas
1	4200402
2	4186308
3	4199120
4	4184070

5	4203797
Mean	4194739
% RSD	0.2

Table 9: Method Precision

S.NO	Percentage Assay
1	98.0
2	96.0
3	96.4
4	96.1
5	97.9
6	97.7
Mean	97.0
% RSD	1.0

Table 10: Robustness

SAMPLE TYPE	%ASSAY
Flow 0.8ml(spl-1)	99.5
Flow 0.8ml(spl-2)	99.4
Flow 1.2ml(spl-1)	99.8
Flow 1.2 ml(spl-2)	99.2
pH 2.8 (spl-1)	99.5
pH 2.8 (spl-2)	99.1
pH 3.2 (spl-1)	99.2
pH 3.2 (spl-2)	99.0
240nm(spl-1)	99.2
240nm(spl-2)	99.2
244nm(spl-1)	99.3
244nm(spl-2)	99.0
Average	99.3
SD	0.22
%RSD	0.23

Table 11: Solution stability of standard

TIME(HOURS)	PEAK AREA	CUMULATIVE % RSD
Initial	4211010	
4	4290684	1.2
8	4240415	0.8
12	4310783	1.1
16	4399875	1.6
20	4352040	1.7
24	4338045	1.4

Table 12: Solution stability of Sample

TIME(HOURS)	PEAK AREA	CUMULATIVE % RSD
Initial	4172514	
4	4112804	**1.0**
8	4177426	**0.9**
12	4218648	**1.0**
16	4232835	**1.1**
20	4205063	**1.0**
24	4228953	**1.0**

Analysis Of Formulation

S.No.	Drug	Label Claim(mg)	Amount found (mg)	Assay %RSD
1	Ibuprofen	25	24.79	99.4

Accuracy

Parameters	Ibuprofen
Linearity Range (µg/spot)	0.1-0.5
Slope	6891.5
Intercept	20.94
Regression coefficient	0.999

Table 16: Recovery study for Ibuprofen n=3

Label claim	Recovery level %	Amount added	Amount recovered	% recovery
200	80	150	149.89±0.78	99.89
200	100	200	199.78±0.97	99.91
200	120	250	250.51±0.51	101.6

Table 17: precision of Ibuprofen

S.No	Concentration (µg/ spot)	Peak area
1	0.3	2082.98
2	0.3	2111.50
3	0.3	2087.23
4	0.3	2077.31
5	0.3	2081.23
6	0.3	2091.17
Mean	-	2088.57
Percentage Relative standard deviation	-	0.57

Table 18: Intra-day Precision of Ibuprofen

S.No	Concentration	Area	Mean	Standard deviation	%RSD
1	0.1	755.34	756.73	3.29	0.43
2	0.1	761.08			
3	0.1	753.78			
1	0.3	2082.98	2081.989	2.73	0.12
2	0.3	2083.98			
3	0.3	2078.98			
1	0.5	3470.7	3471.37	5.12	0.12
2	0.5	3467.70			
3	0.5	3475.71			

Table 19: Inter day Precision of Ibuprofen

S.No	Concentration	Area	Mean	Standard deviation	%RSD
1	0.1	757.34	758.73	3.91	0.51
2	0.1	756.08			
3	0.1	761.78			
1	0.3	2081.98	2083.98	6.23	0.34
2	0.3	2090.98			
3	0.3	2078.98			

Figure 1: HPLC Chromatogram profile of Ibuprofen

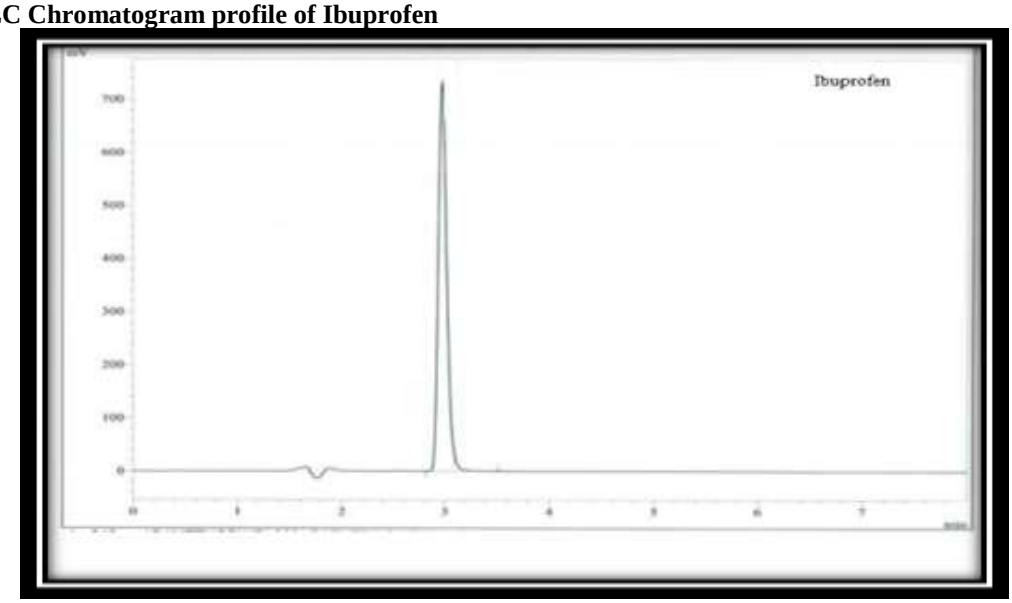


Figure 2: Calibration curve of Ibuprofen

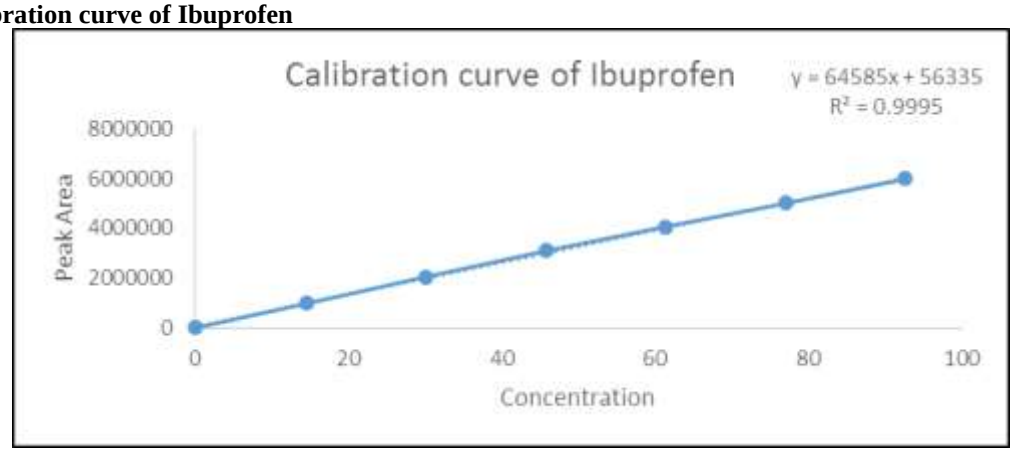


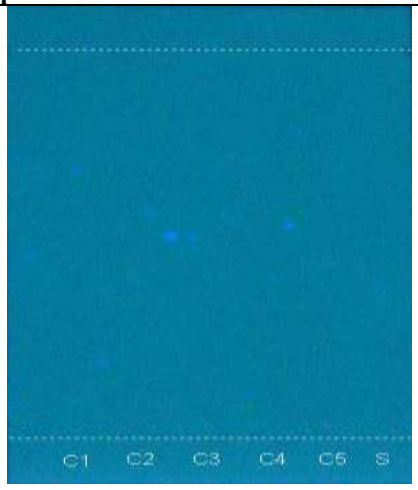
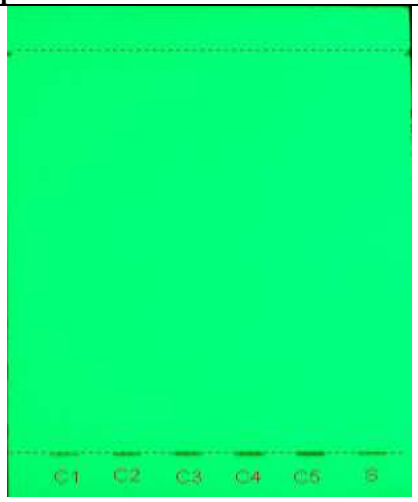
Figure 3: Daylight before mobile phase run	Figure 4: UV 366nm before mobile phase run	Figure 5: UV 254 nm before mobile phase run
		

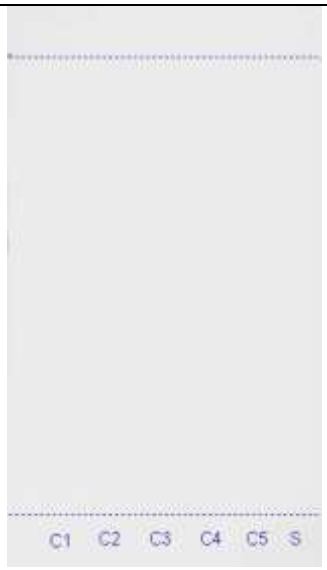
Figure 6: Daylight after mobile phase run	Figure 7: UV 366nm after mobile phase run	Figure 8: UV 254 nm after mobile phase run
		

Figure 9: Linearity of Ibuprofen

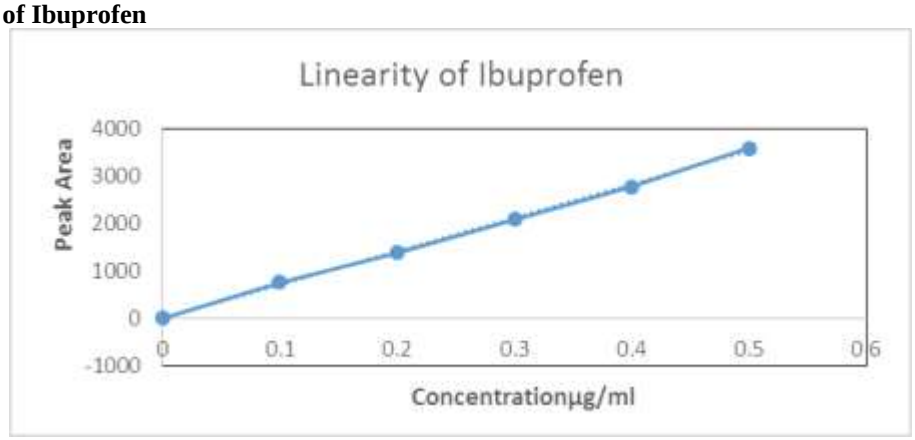


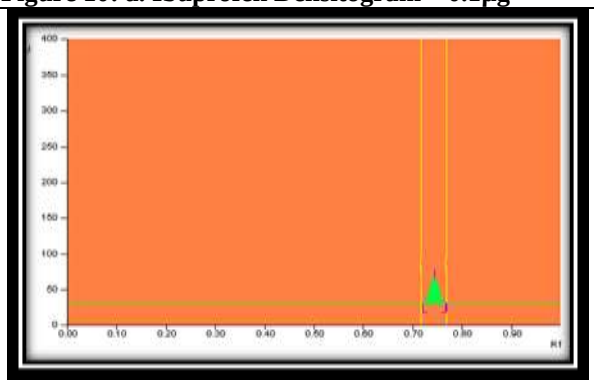
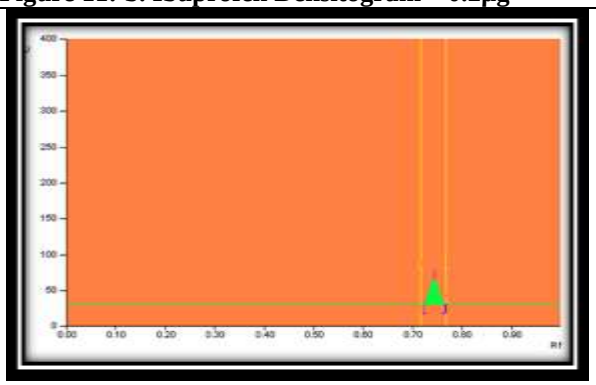
Figure 10: a. Ibuprofen Densitogram – 0.1µg	Figure 11: b. Ibuprofen Densitogram – 0.2µg
	

Figure 12: c. Ibuprofen Densitogram – 0.3µg

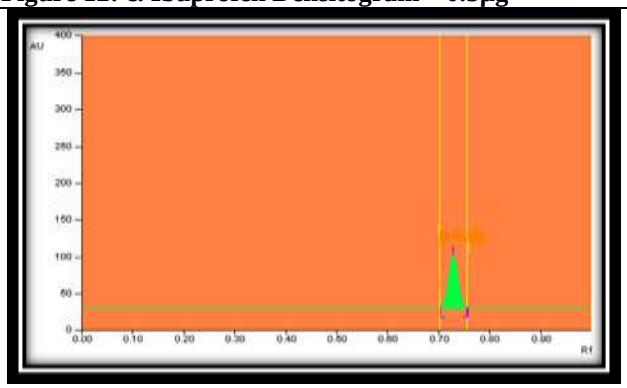


Figure 13: d. Ibuprofen Densitogram – 0.4µg

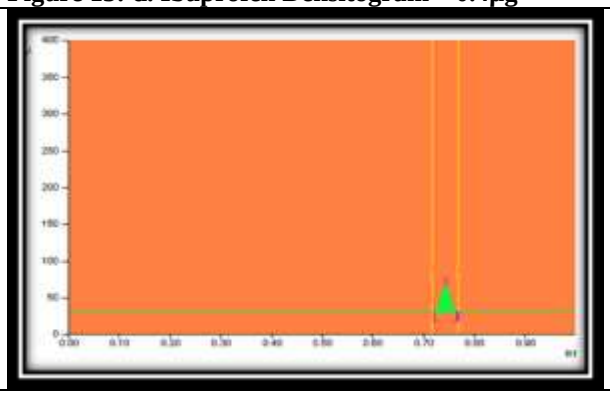


Figure 14: e. Ibuprofen Densitogram – 0.5µg

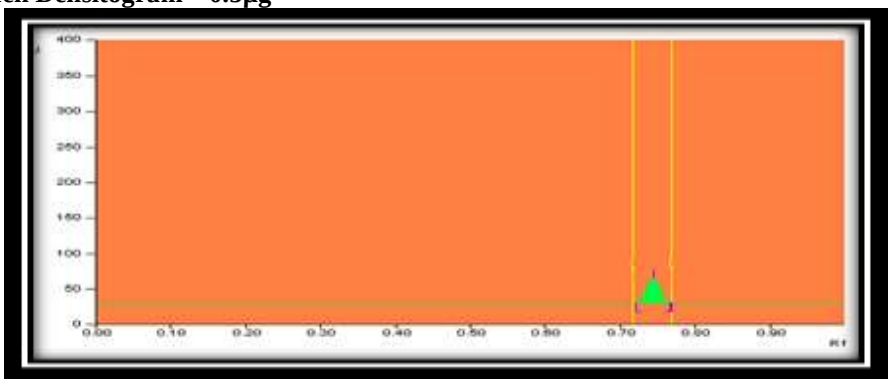


Figure 15: Linearity of Ibuprofen

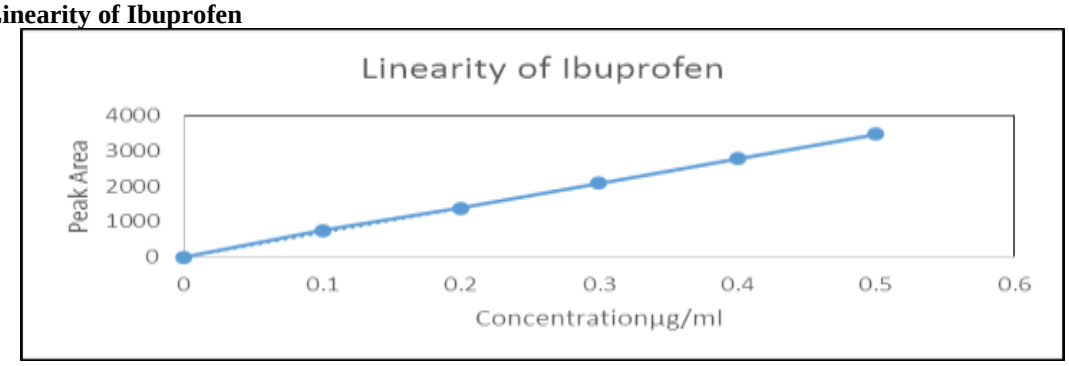
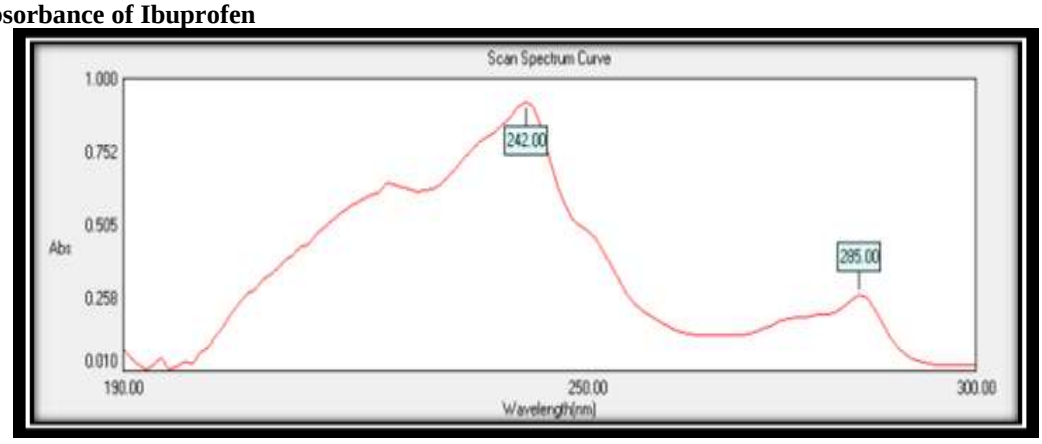


Figure 16: Absorbance of Ibuprofen



Quantification of Ibuprofen In Formulation

A volumetric flask containing 100ml of ibuprofen was filled with an aliquot quantity equal to 100mg of ibuprofen weighing an average weight of 20 tablets of ibuprofen. It was then diluted to obtain the stock solution with a concentration of 50µg/ml by shaking the contents with methanol so as to dissolve the active ingredients. The resultant solution was diluted to 50 ml and scanned in the wavelength range of 200-400nm to measure its absorbance. 3 ml of the resultant solution was taken and diluted to 3 µg/ml.

CONCLUSION

As a result of the observations made regarding the validation parameters, such as accuracy, precision, specificity, and linearity, it can be concluded that the developed methods can be utilized to carry out routine analyses on bulk and tablet forms of carvedilol. There was a compliance with the ICH and USP guidelines as well as the BEER's law as a result of the validation parameters

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