RESEARCH PAPER

ANALYTICAL METHOD DEVELOPMENT AND VALIDATION OF GASTROINTESTINAL DRUG IN BULK AND PHARMACEUTICAL DOSAGE FORM

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ABSTRACT:
The present study involve the development and validation of a simple, accurate, precise, and robust by RP High-Performance Liquid Chromatography (HPLC) these method use for the quantitative estimation of Fexuprazan Hydrochloride in bulk drug and pharmaceutical dosage forms. Various method were perform to validate the developed method various chromatographic condition are perform for the validation . Chromatographic separation was done by using a mobile phase consisting of methanol and 0.1% acetic acid in the ratio of 60:40 (% v/v), with detection perform at 220 nm.solubity study were perform optimization of HPLC are perform. The method demonstrated satisfactory chromatographic performance with good peak symmetry and acceptable retention characteristics. The developed method was validated according to the ICH guidelines. its involve the the graph result of validation parameter such as . The linearity, accuracy, precision Range, Specificity etc Hence the method was found to be simple, accurate, precise, economic and reproducible. So the proposed methods can be used for the routine quality control analysis Fexuprazan in bulk formulations. The developed RP-HPLC method for estimation of Fexuprazan is accurate

KEYWORDS:
Fexuprazan Hydrochloride, HPLC, Validation, ICH Guidelines, Assay , Wavelength , Analytical Method Development.
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INTRODUCTION:

Gastrointestinal disorders are the most common and major health related condition that affect the people health widely Following are the Conditions such as gastroesophageal reflux disease (GERD), peptic ulcer disease, and erosive esophagitis are mainly caused by excessive gastric acid secretion and can cause to symptoms like heartburn, acid reflux, stomach pain, and discomfort. If not treated properly, it affect the patient's quality of life and health serious complications.[1-2] Therefore, effective medications that control gastric acid secretion play an important role in the management of these disorders.[3-4-5]

Fexuprazan is a new potassium-competitive acid blocker (P-CAB) that decrease the gastric acid secretion it block the H^+/K^+-ATPase enzyme that are present in the stomach. It produce rapid and long-lasting acid suppression, it is effective treatment for acid-related gastrointestinal diseases. [6-7]This enzyme plays important role in production hydrocloric acid fexuprazan acts on the proton pump itn bind to the potassium-binding site. [8-9] This action results in rapid inhibition of acid secretion it produce a faster onset of therapeutic effect.As the use of Fexuprazan increases, it is important to develop accurate analytical methods to ensure the quality, safety, and effectiveness of its pharmaceutical formulations.[10-11]

Analytical method development is an important step in pharmaceutical research because it helps devolop a suitable procedure for the accurate estimation of a drug in its dosage form.[12-13] A well-developed analytical method should be simple, accurate, precise, reproducible, and suitable for routine quality control. After method development, validation is carried out to confirm that the method consistently provides reliable and reproducible results under the specified conditions.[14-15]

According to the ICH guidelines of the , analytical method validation includes the evaluation of

parameters such as specificity, linearity, accuracy, precision, robustness, limit of detection, limit of quantification. [16 -17-18]The present study aims to develop and validate a simple, accurate, precise, and cost-effective RP-HPLC method[19-20]

MATERIALS AND METHOD:

DRUG PROFILE

- Generic Name: Fexuprazan
- Chemical Name: 2-[(2-fluorophenyl)methyl]-N-(4-(1-methyl-1H-imidazol-2yl)phenyl)acetamide
- Molecular Formula: C20H20FN3O
- Molecular Weight: 337.39 g/mol
- Drug Class: Potassium-Competitive Acid Blocker (P-CAB)
- Category: Anti-ulcer agent

Fig no. 1: Stucture of Fexuprazan

Mechanism of Action

The mechanism action of Fexuprazan is to reduce the gastric acid secretion by blocking the potassium-channal (P-CAB) that selectively and reversibly inhibiting the gastric H^+/K^+-ATPase enzyme, commonly known as the proton pump, lit present on the secretory membrane of gastric parietal cells.

MATERIALS

- Active Pharmaceutical Ingredient (API): Fexuprazan (working standard)
- Formulation: Fexuclave tablets (40 mg), manufactured by Sun Pharma Laboratories

Instrumentation

Table No. 1: HPLC System

HPLC System	**Agilent Tech Gradient System with Auto injector**
Model No	1100
Detector	UV (DAD] Detector
Pump	Quaternary.Gradient G130A) S.NO.DE
Software	ChemStation Software
Column	C18 Column 4.6 x 250 m

Method Development

Solubility Studies

Solubility studies were performed to identify a the solvent in which Fexuprazan is completely soluble. Various solvents such as methanol, acetonitrile, and water were tested. According to results are obtained Fexuprazan is more soluble in methanol

Selection of Wavelength

A standard solution of Fexuprazan was prepared in methanol and scanned in a UV-Visible spectrophotometer over the range of 200–400 nm. The wavelength showing maximum absorbance (λmax) was selected for HPLC analysis. 220 nm was chose

Optimization of HPLC Method

The HPLC method was optimized to develop a reliable and accurate analytical method for the estimation of Fexuprazan in bulk and dosage form.Different mobile phase compositions were tested to achieve good peak shape, resolution, and acceptable retention time. After several trials, the optimized chromatographic conditions were established. Method development

Cromatographic Condition

Fexuprazan was found to be freely soluble in methanol, which was selected as the diluent for the study. Several chromatographic trials were carried out using different mobile phase compositions, flow rates, and detection wavelengths to obtain a sharp, symmetrical peak with good resolution. Optimized chromatographic separation was achieved using a 4.6 × 250 mm analytical column packed with 5 µm particles. The mobile phase consisted of methanol and 0.1% acetic acid (60:40, v/v). The mobile phase was filtered through a 0.45 µm membrane filter and degassed before use. The flow rate was maintained at 0.8 mL/min, and detection was carried out at 220 nm using a UV diode array detector (DAD). The injection volume was 20 µL, and the chromatographic analysis was performed under ambient temperature. Under these optimized chromatographic conditions, Fexuprazan produced a sharp, well-resolved, and symmetrical peak with satisfactory system suitability parameters, demonstrating that the developed RP-HPLC method is suitable for the routine quantitative analysis of Fexuprazan

Solvents Used:

- Methanol (HPLC grade)
- Distilled water
- Acetic acid (Analytical grade)Mobile phase mixing capability: 0–100% (quaternary system)

Selection of Mobile Phase

Table No. 2: Chromatographic Condition for mobile phase

Colum	C 18
Flow rate	07 ml/min
Wavelength	220nm
injection Time	20.0 µL
Mobile phase	Methanol : 0.1% Acetic Acid (60:40, v/v)
Run time	14min
Retention time	3.857 min
Peak Area	46.73885
Telling Factor	0.98
Theoretical plate	4378

Preparation of Mobile Phase

The mobile phase consisted of methanol and 0.1% v/v acetic acid in water in the ratio of 60:40 (% v/v). Preparation of 0.1% v/v Acetic Acid Solution Accurately measured 1.0 mL of acetic acid was transferred into a 1000 mL volumetric flask. The volume was made up to the mark with distilled water and mixed thoroughly to obtain a 0.1% v/v acetic acid solution.

Preparation of Standard Stock Solution

A standard stock solution of Fexuprazan was prepared by accurately weighing 5 mg of Fexuprazan and transferring it into a 10 mL volumetric flask. The drug was dissolved in a small quantity of methanol and sonicated for about 2 minutes to ensure complete dissolution. The volume was then made up to the mark with methanol to obtain a standard stock solution containing 500 µg/mL of Fexuprazan.

Preparation of Working Standard Solutions

Working standard solutions were prepared by transferring 0.1, 0.2, 0.3, 0.4, and 0.5 mL aliquots of Stock-I into separate 10 mL volumetric flasks. The volume was adjusted to the mark with the mobile phase to obtain final concentrations of 5, 10, 15, 20, and 25 µg/mL, respectively. The prepared solutions were mixed thoroughly and used for calibration and chromatographic analysis

Preparation of Tablet Solution

Brand Name: FEXUCLUE 40 mg

Manufacturer: Sun Pharma Laboratories Ltd.

Twenty stablets were accurately weighed and finely powdered. The total weight of the powdered tablets was found to be 1.356 g, and the average weight per tablet was calculated as 67.8 mg.

The quantity of tablet powder equivalent to 5 mg of Fexuprazan was calculated using the formula:

Quantity of Powder Required (mg) = (Amount of Drug Required × Average Tablet Weight) / Label Claim

An accurately weighed quantity of 8.475 mg of tablet powder equivalent to 5 mg of Fexuprazan wasvtransferred into a 10 mL volumetric flask. The powder was dissolved in methanol, and the volume was made up to the mark with methanol to obtain a solution containing 500 µg/mL of Fexuprazan. This solution was designated as Sample Stock Solution (Stock Solution II).

RESULTS AND DISCUSSION:

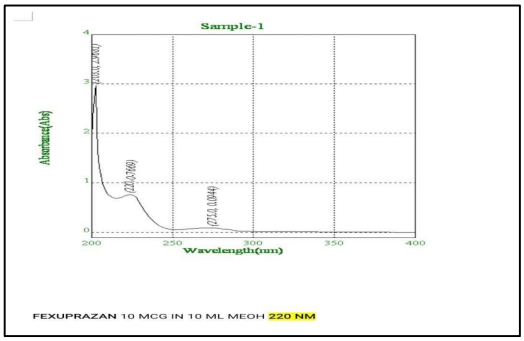

Fig no. 2: UV Visible Graph

VALIDATION PARAMETER:

Linearity

The linearity of an analytical procedure is the ability to obtain test results, which are directly proportional to the concentration of an analyte in the sample. The developed RP-HPLC method exhibited excellent linearity for Fexuprazan The correlation coefficient (R^2 = 0.9991) indicated a strong linear relationship between concentration and peak area, confirming the suitability of the method for quantitative analysis.

Table No. 3: Chromatographic Data for Linearity

Con	Area 1	Area 2	Mean Area	SD	%RSD
5	163.913	164.213	164.063	0.21	0.13
10	355.388	354.932	355.160	0.65	0.18
15	543.731	546.014	544.873	3.23	0.59
20	759.594	760.325	759.960	1.03	0.14

25	972.633	973.179	972.906	0.77	0.08

Table No. 4: regression Equation Data Y=mx+

Slope(m)	40.4725
Intercept (c)	47.3855
Correlation Coefficient	0.9991

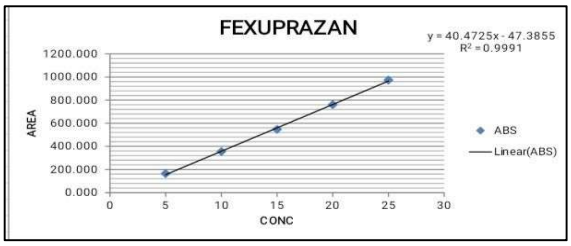

Fig no. 3: Liniarity Graph of Fexuprazan

Accuracy

Accuracy was calculated by the standard addition method at three concentration levels (80%, 100%, and 120%), corresponding to 4, 5, and 6 µg/mL, respectively. Appropriate aliquots of Tablet Stock Solution II and the working standard solution were transferred into separate 10 mL volumetric flasks, and the volume was made up to the mark with the diluent to obtain the required concentrations.

Table No. 5: Chromatographic Data of Accuracy

Area (Mean* ± S.D.)	**Amt. recovered (Mean*±S.D)**	**%Recovery (Mean*±.SD.)**
365.55±1.01	4.03 ± 0.025	100.81%±0.62
404.14±0.04	4.99± 0.01	99.71% ± 0.02
448.19±2.10	6.07 ± 0.052	101.24%±0.87

Table No. 6: Chromatographic Data of Accuracy

Level	**Mean recovery**	**SD**	**%RSD**
80%	100.81	0.62	0.62
100%	99.72	0.02	0.02
120%	101.24	0.87	0.85

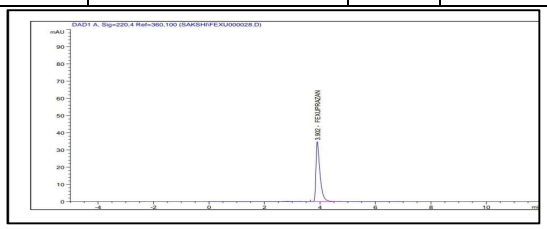

Fig no. 4: Cromatogram of Accuracy 80 %

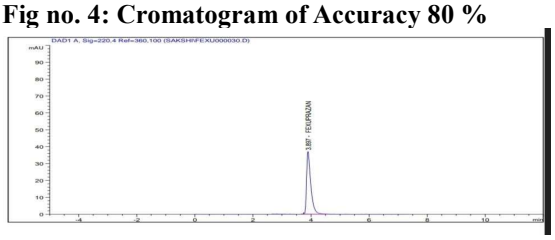

Fig no. 5: Chromatogram of Accuracy 100 %

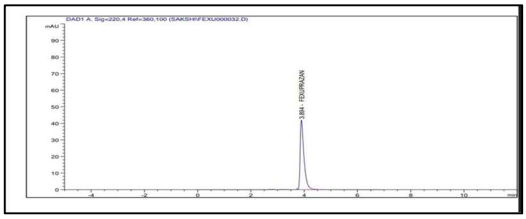

Fig no. 6: Chromatogram of Accuracy 120 %

Table No. 7: LOD and LOQ

Parameter	**Value**
LOD	0.318
LOQ	0.962

Precision

Interday Precision

Precision of the developed RP-HPLC method were evaluated by intraday and interday studies at four concentration levels in. (10, 15, and 20 µg/mL)

Table No. 8: Observation of Intraday Precision

Con	**Area 1**	**Area II**	**III**	**IV**	**V**	**Mean**	**Amt Found**	**AM**	**% Amt Found**	**SD**	

10	364.72	362.24	47.3	40.47	410.87	363.49	10.15	1.015235977	101.52	1.76	0.48
15	553.6466	558.9334	47.38	40.47	603.667	556.299	14.922	0.9944320 9	99.444	3.74	0.67
20	769.0700	766.2224	47.38	40.47	815.003	767.65	20.14	1.006952063	100.70	2.01	0.26

Intraday Precision

Table No. 9: Chromatographic Data of Intraday Precision

Con	Area	III	IIII	IV	V	Mean	Amt Found	AM	% Amt Fnd	SD	%RSD
10	358.4333	357.5066	47.38	40.47	405.335	357.97	10.002	1.00160489 3	100.16	0.66	0.18
15	550.7222	556.9199	47.38	40.47	601.220	553.382	14.886	0.99036405 6	99.04	4.38	0.79
20	769.1577	764.5466	47.38	40.47	814.233	766.85	20.12	1.00596923 6	100.60	3.26	0.43

Robustness

The robustness of the developed HPLC method was evaluated by making small deliberate changes in the mobile phase composition (59:41 and 61:39) and detection wavelength (219 nm and 221 nm). The chromatographic responses showed minimal variation under all modified conditions, with %RSD values below 2%, indicating good reproducibility. .

Table No. 10: Chromatographic Data of Change in Mobile Phase (59:41)

Sr. No.	Concentration (µg/mL)	Peak Area	Parameter	Result
1	5	186.389	Mean	188.78
2	5	187.828	SD	0.71
3			%RSD	0.38

Table No. 11: Observation of Change In Mobile Phase (61+39)

Sr. No.	Concentration	Peak Area	Parameter	Result
1	5	188.278	Mean	188.78
2	5	189.289	SD	0.71
3			%RSD	0.38

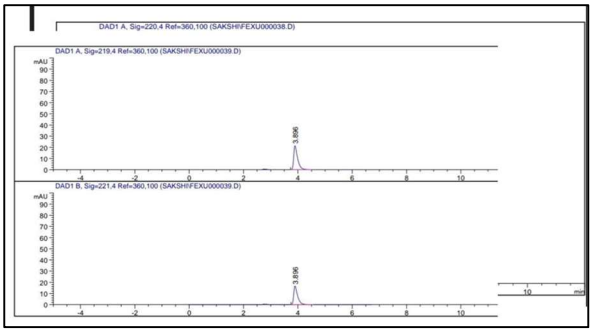

Fig no. 7: Chromatographic Graph of Change in Wavelength (59 +41)

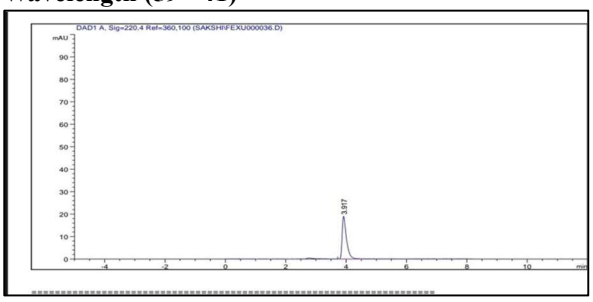

Fig no. 8: Chromatographic Data of Change in Wavelength (61+39)

Change in Wavelength

Table No.12: Chromatographic Result of Wavelength change 219nm

Conc. ugm/ml	Area	Parameter	Result
5	211.225	Mean	211.3
5	211.419	SD	0.14
		%RSD	0.06

Table No. 13: Chromatographic Result of Wavelength change 221 nm

No.	Conc. µgm/ml	Area	Parameter	Result
1	5	163.846	Mean	163.451
2	5	163. 451	SD	0.78
3		1	%RSD	0.

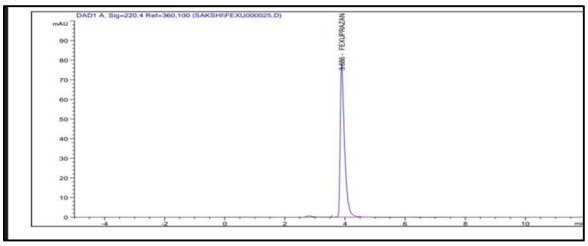

Fig no. 9: change in Wavelength

Specificity

Table No. 14: Cromatographic Data Of Specificity

Sr no.	Conc	Area	Intercept	Slop	Intercept +Area	Amount Found	Labal claim	% claim
1	15	566.254	47.38	40.47	610.49	15.1627	1.010845	101.08
2	15	568.129	47.38	40.47	608.87	15.2090	1.013934	101.39
3	Mean	567.19				15.19		101.24
4	SD	1.326				0.033		0.218
5	RSD	0.234				0.216		0.216

Assay of Tablet

Tab Assay:- Take 20 µ gm/ml for assay (0.2 ml FROM STOCK II AD makes up volume 10ML. Methanol was added, the solution was sonicated, and the volume was made up to the mark. After filtration through a 0.45 µm membrane filter, the solution was diluted to obtain a final concentration of 20 µg/mL. The sample was injected into the RP-HPLC system

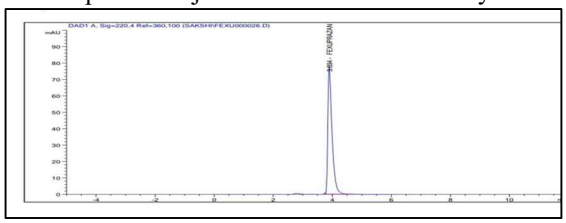

Fig no. 10: Chromatogram of Assay of Tablet 10 MCG

CONCLUSION:

The present work deal with "Development and validation of RP-HPLC method for estimation of fexuprazan in Bulk Drug And it`s Dosage form". The developed RP-HPLC method for estimation of Fexuprazan was found to be simple, accurate, precise, economical, and robust. The validation results were within acceptable limits according to ICH guidelines, confirming the suitability of the method for routine pharmaceutical analysis.

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