

Process Development and Justification for Furosemie

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ABSTRACT

A simple, Accurate, precise method was developed Furosemie tablet dosage form. Chromatogram was run through Discovery Cosmosil C18 (250mm x 4.6ID, Particle size: 5 micron) column at a flow rate of 1 ml/min and the runtime was 4min. The mobile phase consisted of water and acetonitrile in the percentage of 80:20, and elements were scanned using a UV detector at 281 nm. Temperature was maintained at 25°C. Optimized wavelength selected was 235nm. Retention time of Furosemie was found to be 4.078min and 3.455. %RSD of the Furosemie were and found to be 0.8 and 0.4 respectively. %Recovery was obtained as 99.76% and 99.59% for Furosemie respectively. LOD, LOQ values obtained from regression equations of Furosemie were 0.037815088, 0.1145 respectively. Retaining periods were reduced and that run spell was diminished, so the way developed was unpretentious and cost-effective that can be approved in regular Eminence control test in Productions.

Keywords: Furosemie, Converse phase high act liquid chromatography, Filth, Endorsement, ICH

Objective: The contemporary training designates the firmness signifying reverse-phase high- act liquid chromatography (RP-HPLC) process for instantaneous guesstimate of Furosemie.

Methods: The projected RP-HPLC process was established using HPLC Binary Gradient System equipped with UV detector, and chromatographic leave-taking was accepted on Cosmosil C18 (250mm x 4.6ID, Particle size: 5 micron) column at a stream amount of 1 ml/min and the runtime was 4min. The mobile chapter entailed of water and acetonitrile in the proportion of 80:20, and nitty-gritties were scanned with a UV gauge at 281 nm.

INTRODUCTION

Furosemie is a circle diuretic. It is chemically 4-chloro-2-furfurylamino-5- Henle [4]. Furosemie helps to keep potassium and curtail the jeopardy of alkalosis, in the behavior of edema linked with hepatic cirrhosis besides congestive core failure [2,5].

The thorough literature survey reveals that few analytical methods such as RP-HPLC and UV methods are reported out to acquire new, simple, accurate, rapid, and cost-effective firmness representing RP-HPLC process for the immediate guesstimate of Furosemie in pharmaceutical dose form. The suggested method stayed applied ccessfully to divided up the besmirched products from the models.

METHODS

Reagents and chemicals

Furosemie standards were provided by Maharashtra, India, The HPLC mark acetonitrile and sea were obtained from Maharashtra, India,

Instrument

The chromatographic departure was passed out by The wished-for RP-HPLC method was developed using HPLC Binary Gradient System equipped with UV detector, and chromatographic leave-taking was passed on on) column at a stream the runtime was 4min. The movable phase involved of sea of 80:20, and elements detector at 281 nm.

Selection of wavelength

Furosemie drug were scanned by UV individually, in a wavelength range of 200–400 nm and maxima

for each drug was measured. The corresponding UV spectrum graphs of the drugs such as The detection wavelength was selected from the overlay UV spectrum and was create to be 281 nm.

Chromato graphic situations

The chromate graphic departure of analyts was accepted out with HPLC Binary Gradient System equipped with UV indicator, and chromate graphic departure was accepted on Cosmosil C18 pilaster at a stream proportion of 1 min and the runtime was 4min. The mobile phase consisted of water and acetonitrile in the ratio of 80:20, and elements were perused using a UV indicator at 281 nm.

The portable phase of a mix of sea and acetonitrile Mix 800ml of 0.1% Furosemie sea with200 ml of Acetonitrile, Mesh over 0.45 μ and degas it.

The chromatogram was analyzed using different combination of 0.1% Furosemie Acetonitrile: Water { 70:30, 80:20} at current rate of ml/min for at 218nm

The runtime was set at 4 min

Grounding of Standard Result:

Accurately weigh 10 mg Drug added in 10 ml Acetronitrile, get 1000 μ g/ml solution, further dilution done with Diluent.

Grounding of Sample Explanation:

Sample Stock solution:

Weighed 41.7591mg powder equivalent to 10mg of Furosemie, mixed well and Triturate with mortar pestle, transferred into a 100 ml vic flagon. Added about 30 ml diluent, solicited to dissolve the content and

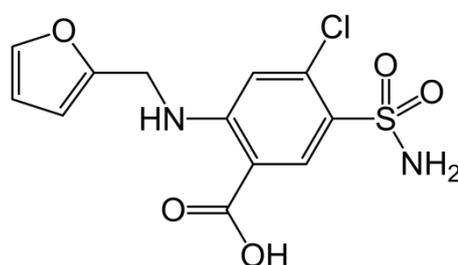
bulk was ended with dilutant. Extra transferred 0.3ml above solution in 10ml solvent in Volumetric Flask, type up the bulk up to 10ml with diluent.

Sample Solution:

0.3mg was added in 10mg of solvent and made volume with diluent (30µg/ml)

Method validation

The method validation was done giving to the ICH strategies with upstairs established RP-HPLC Furosemie. Several strictures were gaged such as society suitability, care, accuracy, segment, strength, limit of finding (LOD), and bound of quantification (LOQ)



Molecular Formula	C ₁₂ H ₁₀ ClN ₂ NaO ₅ S
Molecular Weight	352.73 g/mol
IUPAC name	4-Chloro-2-[(furan-2-ylmethyl)amino]-5-sulfamoylbenzoic acid
Appearance	white to off white yellowish crystalline powder white, round, scored, tablet imprinted with "EP 117" and "40"
Solubility	soluble in acetone (50 mg/ml), yielding a clear to slightly hazy yellow solution hydroxides. Furosemie is practically unsolvable in sea.
Melting Point	203-205 °C
Category	Diuretics
Pka	3.9

Forced degradation studies

The ICH degradation was attempted under various stress settings such as

acerbic, alkaline, oxidation, thermal, humidity, and photolytic conditions to

evaluate the interference of degradation impurities.

Acid, base, and rust dilapidations were performed by totaling chamber for 9 days

Preparation:

Standard Stock solution preparation of 1000ppm of individual drug.

- 10mg of pure treatment liquified in 10ml of solvent (solvent was used as your mobile phase only) this bounces 1000ppm key.

Preparation of Movable Point:

Add 1ml Furosemie into 1000ml Purified water

Mix 800ml of 0.1% Furosemie water with 200 ml of Acetonitrile, Filter through 0.45µ and degas it.

The chromatogram was analyzed using different combination of 0.1% Furosemie Acetonitrile: Water { 70:30, 80:20} at stream rate of ml/min for at 218nm

Preparation of Diluent: Acetonitrile: Water (70:30)

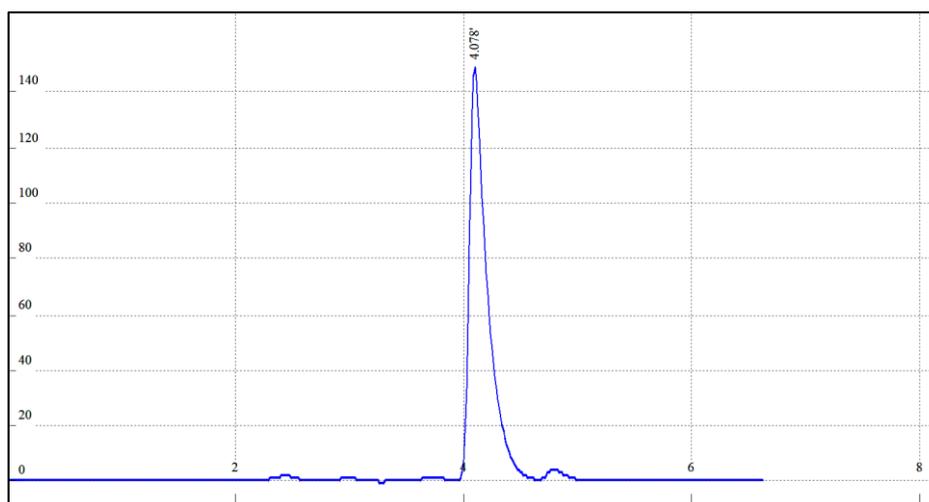
• **Grounding of Standard Explanation:**

Accurately weigh 10 mg Drug added in 10 ml Acetonitrile, get 1000 µg/ml solution, further dilution done with Diluent.

Chromatographic parameters:

Column	:	Cosmosil C18
Flow rate	:	0.8 ml/min
Injection volume	:	20µL
Column oven temperature	:	25°C
Run time	:	6.62min
Mobile Phase (Acetonitrile: Water)	:	80: 20 v/v

Chromatographic Conditions for Trial



Typical Chromatogram of Trial (Finalized Trial)

Time	Area	Resolut.	T.PlateNum	Asymmetry
4.078	1754630	0.00	6857	1.22

Observations:

Peak is good and all parameter are within acceptance criteria.

Conclusion:

Above chromatographic parameter and sample extraction method found satisfactory and also specificity found ok hence above Assay.

RESULT AND DISCUSSION

Optimized Method:

Preparation of Buffer solution:

Standard Stock solution preparation of 1000ppm of individual drug.

- 10mg of pure drug dissolved in 10ml of solvent (solvent was used as your mobile phase only); this gives 10 in the series of

00ppm solution. pH 3 with ortho phosphoric acid. Filter through 0.45µNylon membrane filter.

Research of Mobile Phase:

Standard Stock solution preparation of 1000ppm of individual drug

Methanol volume (80;20 v/v),
Filter and Sonicate for 10minutes.

Preparation of Diluent:

Methanol: Water (80:20) v/v

Acetonitrile: Water (70:30) v/v

Acetonitrile: Water (80:20) v/v

Research of Typical Solution (Furosemie)

Standard Stock solution preparation of 1000ppm of individual drug.

Research of Average solution:

- 10mg of pure drug dissolved in 10ml of solvent (solvent was used as your mobile phase only); this gives 1000ppm solution 7.2 ➤

Method Validation

The following parameters were considered for the analytical method validation of optimized method,

- Breadth and Range
- System Suitability
- Specificity
- Precision
 - Repeatability
 - Intraday precision

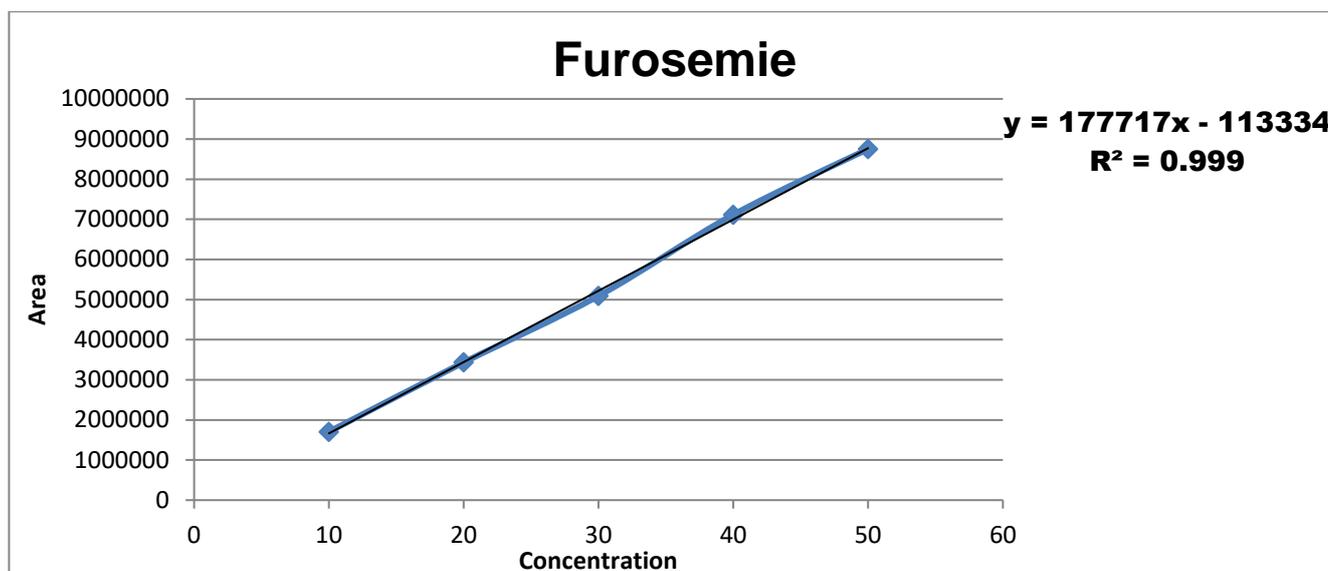
- Inter-day precision

- Accuracy (Recovery)
- Robustness

Breadth and Range

The linearity response was determined by analysing six independent stages of adjustment curve in the succession of 30-180 µg/ml for Furosemie. The stock explanations of usual Fosfomycin were watery to six unlike known focusses. Breadth graph of absorption (as x-value) versus area (as y-value) were plotted and were calculated. And shown in figure7.1and the data obtained summarized in Table.

Conc.	Area	Conc.
10	1704880	10
20	3432462	20
30	5089622	30
40	7113838	40
50	8750024	50
%RSD		53.88%



Linearity Result of Furosemie

Sr. no	Parameter	Result
1	Correction range (µg/ml)	30-180
2	Solvent (Methanol: ACN: Phosphate Buffer)	80:20 /v/v
3	Relapse equation (y*)	$y = 15187x - 13333$
4	Slope (b)	15187
5	Intercept (a)	13333
6	Correlation coefficient(r ²)	0.9994
7	Limit of Detection (µg/ml)	4.9166
8	Limit of Quantitation (µg/ml)	14.89

Table: Characteristic parameters of Furosemie for the projected HPLC way.

System Suitability

besides are used to confirm reasonable performance of the chromatographical organization. The data obtained are summarized.

Sr. No.	Properties	Values
1.	Preservation time	4.078
2.	Area	1754630
3.	Asymmetry	1.22
4.	Theoretical plates	6857

Table: System suitability studies of Furosemie by HPLC method

Specificity:

The outcome of excipients and extra spices usually existing in the dose form of the purpose under finest environments was studied. Furosemie exposed peak at a maintenance time of 6.12 min. The

transportable phase planned for the method resolute the drug very resourcefully. The Preservation stretch of Furosemie was 6.12 ± 0.0098 min. The crowning for Furosemie from the capsule formulation was Furosemie.

Sr. No.	Sample name	Observation
1	Blank	No interference

Table: Results of Specificity study

Precision:

The normal for the six purposes was designed along thru the % RSD for the copy determinations. Mutually the system care and method meticulousness were subjected for inter-day and intra-day distinctions as reported in Table.7.5 and

Repeatability Table

Intraday	Day 1			Day 2		Mean	%RSD
5089622	5085584	5078382	5073366	5084052	5083895	5083895	0.11%

Table: Inray and Inter Care of Furosemie

Intraday	Morning			Evening		
	5089622	5085584	5078382	5085149	5047670	5073701

Table: Repeatability studies of Furosemie

Correctness and Salvage:

Recapture studies by the typical addition method were completed with a view to justify the accurateness of the planned standard and the blends were the % recovery and % RSD stayed calculated and conveyed in Table

process. Previously analyzed samples of Furosemie (120 µg/ml) were spiked with 8, 10, and 20 % extra Furosemie

Sr. NO.	% Composition	Area of Average	Area of Model	% Salvage	%Mean Recovery
1	50% Recovery	5089622	5059707	99.41223533	99.4122353
2	100% Recovery	7113838	7109576	99.9400886	
3	150% Recovery	8750024	8739656	99.8815089	

Table: Recovery of Furosemie

LOD and LOQ:

$$\text{LOD} = \frac{3.3 \times \text{Std. Deviation}}{\text{Slope}}$$

1) LOD :

$$\text{LOD} = \frac{3.3 \times 2036.48}{177717} = 0.037815088$$

$$\text{LOQ} = \frac{10 \times \text{Std. Deviation}}{\text{Slope}}$$

$$\text{LOQ} = \frac{10 \times 2036.48}{177717}$$

2) LOQ

$$= 0.1145$$

Research of Sample Result:

Sample Stock solution:

Weighed 41.7591mg powder equivalent to 10mg of Furosemie, mixed well and Triturate with mortar pestle, transferred flask. Added about 30 ml diluent, solicited to dissolve the content and dimensions stood

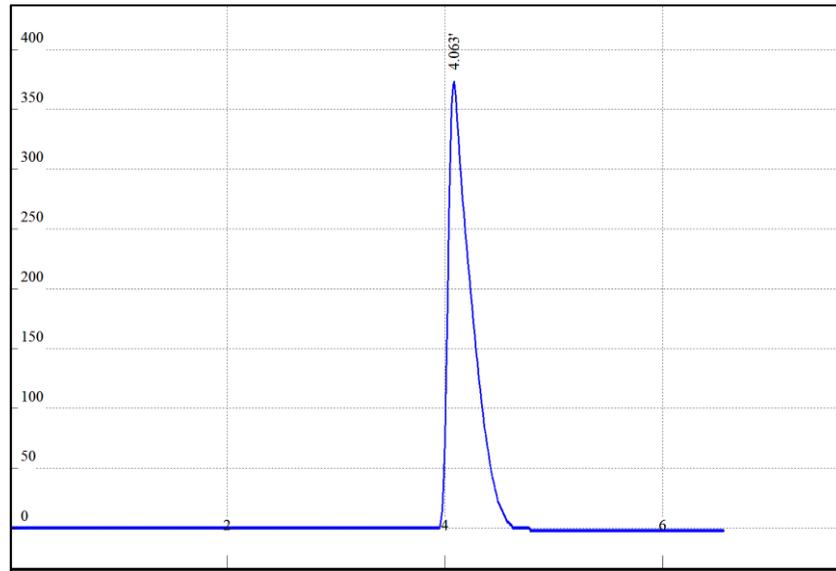
made with diluent. Further transferred 0.3ml above solution in 10ml solvent in Volumetric Flask, make up the volume up to 10ml with diluent.

Sample Solution:

0.3mg was added in 10mg of solvent and made volume with diluent (30µg/ml)

Column	:	Cosmosil C18
Flow rate	:	0.8 ml/min
Injection volume	:	20µL
Column oven temperature	:	25°C
Run time	:	4.063
Mobile Phase (Acetonitrile: Water)	:	80: 20 v/v

Furosemie 30 ppm of formulation



Sample Name: Furosemie 30 ppm of formulation

Wavelength: 233nm

Mobile Phase: Acetonitrile: Water (80:20)

pH of Movable Point: 3 (pH is adjusted with o-phosphoric acid)

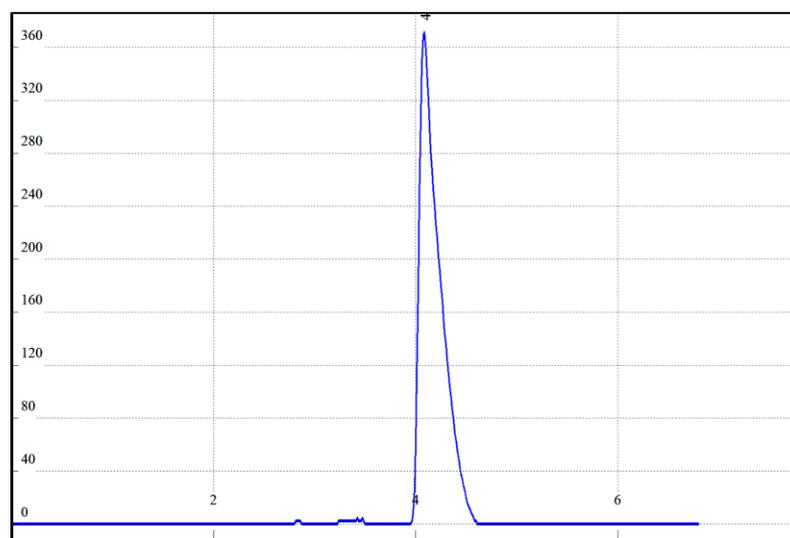
Sample volume: 20µl

Flow rate: 0.8 ml/min

Pressure: 9-10MPa

Run time: 6.56min

Time	Area	Resolut.	T.PlateNum	Asymmetry
4.063	5057264	0.00	7744	1.19



Sample Name: Furosemie 30 ppm 01

Wavelength: 233nm

Mobile Phase: Acetronitrile: Water (80:20)

pH of Movable Phase: 3 (pH is adjusted with o-phosphoric acid)

Sample volume: 20µl

Flow rate: 0.8 ml/min

Pressure: 9-10MPa

Run time: 6.80min

Time	Area	Resolut.	T.PlateNum	Asymmetry
4.063	5089622	0.00	7846	1.15

Sr. NO.	% Composition	Area of Standard	Area of Sample	% Assay
1	% Assay	5089622	5057264	99.3642

SUMMARY AND CONCLUSION

SUMMARY:

Validated analytical methods are aimed for the estimation of Furosemie in formulation. Simple, precise, rapid, accurate methods were Furosemie in formulation by following methods. Estimation of Furosemie by RP-HPLC. Estimation of Furosemie by HPTLC. Estimation of Furosemie by UV-spectroscopy. In RP-HPLC process, a wavelength of 23 nm was particular and the portable point which consist acetonitrile: Water in the percentage of (80:20). pH 3 adjusted with o-phosphoric acid optimum condition for analysis. The retention time was start to be 4.078 with optimized conditions. Furosemie showed the linearity in the choice of 10-50 μ g/ml. Where the peak shape was symmetrical and a good connection factor value was obtained. The percentage label claim and recovery at three diverse stages, 50%, 100%, 150%, level was carried out. The fittingness of the development was thus proved. Care of the process was calculated by construction repeated injection of the same sample and standard deviation was determined. Inter day and intra day precision was also passed out and % RSD was planned. The linearity of drug was determined by correction curve and the segment based on the area observed

in the μ g/ ml. The regression coefficient value for Furosemie is 0.999. Interday precision of the treatments was studied.

CONCLUSION:

Review of fiction on drug sturdily displays that near is few process offered for purpose and confirmation of Furosemie in comprehensive and remedial dosage forms . Care in this cognizance we established methods for courage and confirmation of Furosemie in comprehensive and health dose systems by RP- HPLC, UV devices with some perfections than the prevailing methods. The diagnostic technique designated for assay was explicit, linear, precise, accurate, and arrangement suitable for purpose of Furosemie in across-the-board and pharmacologic dose arrangements. The observations of the validation restrictions such as exactness, precision, specificity, linearity, shows that the established diplomacies can be busy for routine examination of bulk and tablets form of Furosemie. The consequence found from the validation limitations got the ICH and USP prerequisite as shining as sees BEER'S law.

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