Available online at http://ajprd.com

Asian Journal of Pharmaceutical Research and Development

(An International Peer-Reviewed Journal of Pharmaceutical Research and Development)

Open Access to Pharmaceutical and Medical Research

Open Access Research Article

DEVELOPMENT AND OPTIMIZATION OF IMMEDIATE RELEASE TABLET OF FEBUXOSTAT IN GOUT TREATMENT

***Hitesh R. Patel, Dharmik Rami**

S. K. Patel College of Pharmaceutical Education and Research, Ganpat University, Gujarat, India

ABSTRACT

The Formulated Immediate Release tablet based was established by wet granulation techniques. The Optimized tablet were film coated for taste masking of unpleasant taste of Febuxostat drug to improve its patient compliance. The tablets were evaluated for pharmacopoeial and non pharmacopoeial (industry specified) tests. Based on the results, formulation F4 having optimized concentration of crosscarmellose sodium was identified as better formulation among all formulations developed for immediate release tablets. F4 Decrease in binder quantity and increase in disintegrant quantity and remaining all physical parameters of tablets were found satisfactory. Flow of blend was good. Disintegration time and dissolution found comparable to the reference product. Uniformity of dosage units found satisfactory. Further optimization had done by 10 more batches using different concentration of diluents, binders, lubricant, disintegrating agent & glidant and final batches was selected. The result arrived in this work indicates the immediate release formulation of Febuxostat developed in this work was found to be equivalent to reference product, based on the in-vitro Release studies and other evaluation parameters envisaged the objectives of work.

Keywords: *Immediate Release tablet, Gout, Febuxostat, Optimization, In-vitro release studies*

Cite this article as:

Patel R Hitesh, Development and Optimization of Immediate Release Tablet of Febuxostat in Gout Treatment, Asian Journal of Pharmaceutical research and Development.2018;6 (1):16-25

***Address for Correspondence**

Hitesh R. Patel, S. K. Patel College of Pharmaceutical Education and Research, Mehsana-Gozariya Highway Ganpat University, Gujarat, India

INTRODUCTION:

Oral drug delivery method is the straight forward method and it conveys the least complex for controlling medication. In that way, new compound elements is greater and work in progress now a day's its utilized as a strong dose of the frame it is begin reproducible and compelling in vivo plasma focus after oral organization. For the conventional delivery of drugs mainly most popular & successfully the oral route of drug administration is used. In adherence to an esophagus and dysphasia physical obstacles may cause gastrointestinal ulceration. The dosage form like capsule, tablet are produce difficulty to swallowing them for young adult because of development is incomplete in nervous system, muscular and the elderly patient suffer from dysphasia. The Tablets provide best protection to drug with light, heat, oxidation and stress during transportation with several advantages [1].

Gout is a form of inflammatory arthritis shown in Figure 1. It may also result in kidney stones, or urate nephropathy. Gout is due to high levels of uric acid in the blood due to a combination of diet and genetic factors. At high levels, uric acid crystallizes in surrounding tissues, resulting in an attack of gout. Gout occurs more commonly in those who eat a lot of meat, drink a lot of beer, or are overweight. Diagnosis of gout may be confirmed by seeing the crystals in joint fluid or tophus.

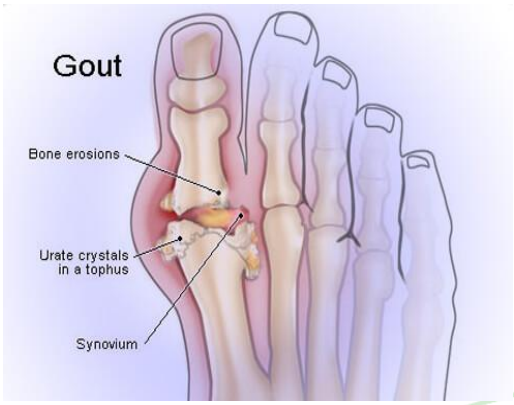

Figure 1: The Anatomy of Gout

The Febuxostat (drug) is a BCS class II drug. The drugs of this class have a high absorption number but a low dissolution number. The absorption for Class II drugs is usually slower than for Class I and occurs over a longer period of time. The Febuxostat is a 2-arylthiazole derivative that achieves its therapeutic effect of decreasing serum uric acid by selectively inhibiting xanthine oxidase. It is a potent, non-purine selective inhibitor of xanthine oxidase (NP-SIXO) with an *in vitro* inhibition k_i value less than one nanomolar and has been shown to potently inhibit both the oxidized and reduced forms of xanthine oxidase[2]..

Equipments:

Table I. Name of the equipment with Unit operation and capacity

Unit operation	Name of the equipment	Capacity
Co-milling	Quadro Co-mill equipped with 0.813 mm screen	
Granulation (Dry and Wet)	Rapid mixer granulator	65L
Wet milling	Quadro Co-mill equipped with 6.350 mm screen	
Drying	Fluid bed dryer	30 kg
Sifting and milling	Sifter equipped with #24 sieve Quadro Co-mill equipped with 1.143 mm screen	-
Blending & Lubrication	Conta Blender	120 L
Compression	Rotary compression machine with force feeder and 'D' tooling	-

Methods:

Preformulation studies

Preformulation studies are the first step in the rational development of dosage form of a drug substance. The objective of preformulation studies is to develop a portfolio of information about the drug substance, so that this information useful to develop different dosage forms.Preformulation can be defined as investigation of physical and chemical properties of drug substance alone and when combined with excipients. [3]

- Identification of drug by FTIR
- Organoleptic characteristics
- pH solubility of drug
- Particle size distribution
- Physico-mechanical characteristics
- Hygroscopicity study
- Compatibility study

Materials and methods

Materials:

Lactose Monohydrate(Pharmatose 200 M): DFE pharma Pvt Ltd; Microcrystalline Cellulose (Comprecel M 101D+): DFE pharma Pvt Ltd; Croscarmellose Sodium (Acdisol): Signetchemical corporation pvt Ltd; Hydroxy propyl cellulose (Klucel LF): DFE pharma Pvt Ltd; Magnesium Stearate (Veg. Grade): Dr. paul lohman; Opadry Yellow 15B520054: Colorconasia pvt ltd.

Most of the excipients selected are widely used in oral pharmaceutical formulations and are from reputed international manufacturers. Excipients selection was based on the previous experience of the mentioned excipients, reliability of the supplier source, their recommendations, and their compliance with Ph.Eur. standards. All the excipients were tested and found to be complying with the Ph. Eur. Monographs except Opadry Yellow 15B520054 complies with in-house specification. The formulation was developed using excipients similar to reference or the functionality was equivalent to reference product.

Preliminary trials (Immediate release formulation):

The formulation development trials for Febuxostat tablets 120 mg and 80 mg was performed. The wet granulation process was method of choice by considering poor flow of drug substance. The table below provides summary of trials conducted for prototype formulation selection. The proto-type formulation selection was done based on dissolution mapping with the reference product and uniformity of dosage units.

The tablets were manufactured for Four batches F1 to F4 using different ratios of superdisintegrants mentioned in the keeping the total weight (120 mg) of the tablet constant in all the formulations. Febuxostat tablets were prepared by directs compression technique as per the formula given in the Table 5.2. The superdisintegrants such as croscarmellose sodium, crospovidone and sodium starch glycolate were used in different proportions.

Table II. Summary of prototype formulation composition

Sr. No.	Ingredients	120 mg strength (Batch No)			
		120-F01	120-F02	120-F03	120-F04
	Intra granular part				
1	Febuxostat	120.00	120.00	120.00	120.00
2	Lactose Monohydrate (Pharmatose 200 M,DMV)	120.00	120.00	120.00	120.00
3	Microcrystalline Cellulose (Comprecel M 101D+)	195.00	195.00	292.00	290.00
4	Croscarmellose Sodium (Acdisol)	9.00	9.00	12.00	10.00
5	Hydroxy propyl cellulose (Klucel LF)	20.00	20.00	20.00	20.00
6	Purified Water*	q.s.	q.s.	q.s.	q.s.
	Extra granular part				
7	Microcrystalline Cellulose (Comprecel M102)	264.00	278.00	168.00	167.00
8	Croscarmellose Sodium (Acdisol)	40.00	25.00	25.00	30.00
9	Silica, Colloidal Anhydrous (Aerosil 200)	3.50	4.00	4.00	4.00
10	Magnesium Stearate (Veg. Grade)	3.50	4.00	4.00	4.00
	Total weight of uncoated tablets	775.00	775.00	765.00	765.00
11	Opadry white 03F580010	19.60	19.60	-	-
12	Ferric oxide yellow	0.40	0.40	-	-
13	Opadry yellow 03F82751	-	-	15.00	-
14	Opadry yellow 32K520080	-	-	-	15.00
15	Purified water	q.s.	q.s.	q.s.	q.s.
	Total weight of coated tablets	**795.00**	**795.00**	**780.00**	**780.00**

All the ingredients were passed through sieve #40 and were subjected for drying to remove moisture content at 40 to 45^{0}C. Weighed amount drug and excipients except magnesium stearate and talc were mixed properly by geometric addition method for 20 minutes manually. Talc and magnesium stearate were then passed through sieve #80, mixed and blended well with the initial mixture. The mixed blend of drug and the excipients were compressed on Karnavati 10 station rotary punching machine using 2 mm diameter round concave punch (force used: 58.5 kN).

Table III. Summary of process selection and prototype formulation development

Batch Number	Batch Size	Objective	Composition/ Process change	Conclusion
120-F01	600 tablets	Feasibility trial batch of Febuxostat tablets 120 mg using aqueous hand granulation process.	Wet granulation	All physical parameters of tablets were found satisfactory. Flow of blend was good. Disintegration time was low as compared to the reference product.
120-F02	1250 tablets	Trial batch of Febuxostat tablets 120 mg using aqueous wet granulation process in rapid mixer granulator by decrease in disintegrant quantity extra-granularly.	Decrease in disintegrant quantity / Wet granulation	All physical parameters of tablets were found satisfactory. Flow of blend was good. Disintegration was faster as compared to the reference product. However, dissolution found comparable to the reference product. Acceptance value of Uniformity of dosage unit test of test product was found on higher side.
120 - F03	3000 tablets	Trial batch of Febuxostat tablets 120 mg using aqueous wet granulation process using	Increase in binder quantity / Wet	All physical parameters of tablets found satisfactory. Flow of blend was good.

		increase in binder quantity.	granulation	Disintegration time and dissolution found comparable to the reference product. However, test product shows slow release at initial time point. Uniformity of dosage units found satisfactory.
120-F04	3000 tablets	Trial batch of Febuxostat tablets 120 mg using decrease in quantity of binder and increase in quantity of disintegrant.	Decrease in binder quantity and increase in disintegrant quantity/ Wet granulation	All physical parameters of tablets were found satisfactory. Flow of blend was good. Disintegration time and dissolution found comparable to the reference product. Uniformity of dosage units found satisfactory.

Formulation Optimization of different Excipients-
Formulation optimization trials were taken in critical consideration of raw materials which affect drug product. Trials for selection of binder, lubricant, disintegrant and diluent level were studied during formula optimization.
Optimization trials were taken by changing amount of binder, lubricant, disintegrant and diluent level in formulation (± 20 % w/w) with respect to Batch No.120-F04 and its quantity was compensated with diluent, and as a result total weight of core tablets remains same for all optimization batches. The processing was carried out by keeping the parameters as much as similar to batch No. 120-F04 and hence not depicted here. Observations were recorded for physical and chemical characterization. Samples were analyzed for the rate of release in pH 6.8 phosphate buffer.
The impact on the quality of the uncoated tablet has been evaluated for

- Optimization of Diluent concentration
- Optimization of Disintegrant concentration
- Optimization of Binder concentration
- Optimization of Glidant concentration
- Optimization of Lubricant concentration

Evaluation of Immediate release Tablets
The tablets were evaluated for in process and finished product quality control tests i.e. appearance, dimensions , weight variation, hardness,friability and drug content.

Appearance
The tablet should be free from cracks, depressions, pinholes etc. The color and the polish of the tablet should be uniform on whole surface. The surface of the tablets should be smooth.

Dimensions
The dimensions of the tablets are thickness and diameter. The tablets should haveuniform thickness and diameter. Thickness and diameter of a tablet were measured using vernier calipers. These values were checked and used to adjust the initial stages of compression.

Uniformity of weight (Weight variation test)
This is an important in-process quality control test to be checked frequently (every half an hour). Corrections were made during the compression of tablets. 20 tablets were weighed individually. Average weight was calculated from the total weight of all tablets. The individual weights were compared with the average weight. The percentage difference in the weight variation should be within the permissible limits (+ 10%).[4]

Hardness test
Hardness is a force required to break a tablet across the diameter. The hardness of a tablet is an indication of its strength. The tablet should be stable to mechanical stress during handling and transportation. The degree of hardness varies with the different manufactures and with the different types of tablets. The force is measured in kilograms. The hardness was tested using Dr. scheuilnger hardness tester. "Hardness factor", the average of the six determinations, was determined and reported. [5]

Friability test
Friability is the loss of weight of tablet in the container/package, due to removal of fine particles from the surface. This in-process quality control test is performed to ensure the ability of tablets to withstand the shocks during processing, handling, transportation, and shipment. Roche friabilator was used to measure the friability of the tablets. It was rotated at a rate of 25 rpm. Ten tablets were weighed collectively and placed in the chamber of the friabilator. In the friabilator, the tablets were exposed to rolling, resulting from free fall of tablets within the chamber of the friabilator. After 100 rotations (4 minutes), the tablets were taken out from the friabilator and intact tablets were again weighed collectively. Permitted friability limit is 1.0%.[6]

Dissolution
Medium: 0.01N hydrochloric acid; 900 ml. Apparatus 2: 50 rpm. Time: 30 minutes. Procedure : Determine the amount of C21H31N502.HCl dissolved by employing UV absorption at the wavelength of maximum absorbance at about 235 nm on filtered portions of the solution under test, suitably diluted with 0.01N hydrochloric acid, in comparison with a Standard solution having a known concentration of USP Febuxostat Hydrochloride in the same Medium.
Tolerances-Not less than 80% (Q) of the labeled amount of C21H31N502.HC1 is dissolved in 30 minutes.

Remarks-As we had prepared Generic Tablet, we had selected 0.0IN HCL as a dissolution media as per OGD specification. [7]

Tablet disintegration time

The disintegration time (DT) of the tablets was determined in 0.1 N HCl (PH=1.2) at 37 ± 0.5oC using disintegration test apparatus (Electro lab ED-2 Bowl USP, Mumbai). One tablet was placed in each of the 6 tubes of the basket and the time taken for all the tablets to disintegrate and pass through the wire mesh was recorded. The disintegration time should not be more than 15 minutes. Determinations were made in triplicate. An attempt was made to know the drug release mechanism from tablets in different conditions.
The following tests were carried out.

Effect of drying temperature

A batch was fabricated where in drying was carried out at two different during temperature 40°C and 60°C. Both the blends where compressed into tablet and evaluate for dissolution.

Effect of Hardness of the Tablet

It is necessary to see, whether the hardness of the tablets effects on the drug release or not. For this study three types of tablets were prepared, with same powder blend and having same physical parameters but different hardness i.e. 30 N (less hardness), 40 N (standard) and more than 65 N (high hardness). Release study was carried out using USP type II dissolution apparatus (paddle type) at rotational speeds of 50 and 0.01 N HCl as dissolution medium for all three types of tablets varying in hardness. The samples were withdrawn at every 5, 10, 15, 30, 45, 60 minutes and passed through 0.45µm filter. Samples were analyzed at 237 nm in UV-spectrometer. % drug dissolved was calculated. [8]

Loss on drying of coated tablet and Coating uniformity

Loss on drying of the compound measures the percentage content of water present in film coated tablet. 10 tablets were kept at 105°C in Halogen moisture analyzer of Mettler Toledo equipment. From that LOD was noted in table. Samples were taken out at 1, 2, 3% weight build up and evaluated for disintegration test.

Accelerated Stability Study

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time. Under the influence of a variety of environmental factor such as temperature, humidity, light, enabling recommended storage conditions, re-test periods and shelf lives. Generally, the observation of the rate at which the product degrades under normal room temperature requires a long time. To avoid the undesirable delay, the principles of accelerated stability studies are adopted. The international conference on harmonization (ICH) guidelines describes the stability test requirements for drug registration application in the European Union, Japan, and United States of America. The optimized tablets were strip packed. It was then stored at 40°C ± 2°C / 75%RH ± 5% for 4 weeks. The tablets were evaluated for drug content (assay), in vitro drug release profile, related substance, and loss on drying.[9]

Result and Discussion

Feasibility trial batch of Febuxostat tablets 120 mg using aqueous hand granulation process.

Table IV. Batch F01 Physical characterization of tablets

Parameters	Observation
Description	White capsule shaped uncoated tablets engraved with Z95 on one side and plain on other side.
Individual weight (mg)	776 mg – 782 mg
Turret speed (RPM)	25 RPM
Hardness (kp)	24.1 kp – 28.1 kp
Thickness (mm)	5.57 mm – 5.60 mm
Disintegration time	1 minute 25 seconds
Friability	Nil

As show in above table

- All physical parameters of tablets were found satisfactory.
- Flow of blend was found satisfactory
- Disintegration was faster as compared to the reference product.

Trial batch of Febuxostat tablets 120 mg using aqueous wet granulation process in rapid mixer granulator by decrease in disintegrant quantity extra-granularly.

Table V. Batch F02 Physical characterization of uncoated tablets

Parameters	Observation
Description	White capsule shaped uncoated tablets engraved with Z95 on one side and plain on other side.
Individual weight (mg)	775 mg – 780 mg
Turret speed (RPM)	20 RPM
Hardness (kp)	24.5 kp – 27.8 kp
Thickness (mm)	5.68 mm – 5.70 mm
Disintegration time	2 minutes
Friability	Nil

In this batch aqueous wet granulation process was used in rapid mixer granulator by decrease in disintegrant quantity extra-granularly. The effect was observed on acceptance value and disintegration time.

- All physical parameters of tablets were found satisfactory.
- Flow of blend was good.
- Disintegration time was faster as compared to the reference product. However, dissolution found comparable to the reference product.

- Acceptance value of test product was found on higher side.

Trial batch of Febuxostat tablets 120 mg using aqueous wet granulation process using increase in binder quantity.

Table VI. Batch F03 Physical characterization of uncoated tablets

Parameters	Observation
Description	White capsule shaped uncoated tablets engraved with Z95 on one side and plain on other side.
Individual weight (mg)	763 mg – 768 mg
Turret speed (RPM)	25 RPM
Hardness (kp)	24.3 kp – 27.3 kp
Thickness (mm)	5.30 mm – 5.32 mm
Disintegration time	3 minutes 55 seconds
Friability	Nil

In this batch aqueous wet granulation process was used increase in binder quantity so the slow release of the drug was observed.

- All physical parameters of tablets found satisfactory.
- Flow of blend was good.
- Disintegration time and dissolution found comparable to the reference product. However, test product shows slow release at initial time point.
- Uniformity of dosage units was found satisfactory.

Trial batch of Febuxostat tablets 120 mg using decrease in quantity of binder and increase in quantity of disintegrant.

Table VII. Batch F04 Physical characterization of uncoated tablets

Parameters	Observation
Description	White capsule shaped uncoated tablets engraved with Z95 on one side and plain on other side.
Individual weight (mg)	764 mg – 770 mg
Turret speed (RPM)	25 RPM
Hardness (kp)	27.0 kp – 29.7 kp
Thickness (mm)	5.41 mm – 5.43 mm
Disintegration time	3 minutes 10 seconds
Friability	Nil

The formulation of Lower binder concentration nd higher disintegration concentration were developed as F04

- All physical parameters of tablets were found satisfactory.
- Flow of blend was good.
- Disintegration time and dissolution found comparable to the reference product
- Uniformity of dosage units was found satisfactory.

Formulation Optimization of different Excipients

Optimization of diluent level (Microcrystalline cellulose)

Table VIII. Physical parameters of core tablets

Batch No.		**120-F04**	**120-F05**	**120-F06**
Sr.No.	**Parameters**	**Optimum Level**	**Lower Level (-20% w/w)**	**Higher Level (+20% w/w)**
1	Mass of 20 tablets (mg)	15.32	15.33	15.32
2	Individual weight (mg)	765-768	764 – 769	762 – 766
3	Hardness (kp)	23.8-27.0	24.6 – 27.0	24.8 – 26.3
4	Disintegration Time	03minute 20 seconds	03minute 45 seconds	03minute 05 seconds
5	Friability (% w/w)	Nil	Nil	Nil
6	Thickness (mm)	5.13-5.15	5.13 – 5.18	5.11 – 5.16

From the above data, it was concluded that change in microcrystalline cellulose level in studied range had no significant impact on dissolution profile, so concentration of microcrystalline cellulose 290 mg per tablet was selected for final formulation proposed for exhibit batch.

Optimization of disintegrant level (croscarmellose sodium):-

Table IX. Physical parameters of core tablets

Batch No.		120-F04	120-F07	120-F08
Sr.No.	Parameters	Optimum Level	Lower Level (-20% w/w)	Higher Level (+20% w/w)
1	Mass of 20 tablets (mg)	15.32	15.34	15.33
2	Individual weight (mg)	765-768	763 – 768	762 – 766
3	Hardness (kp)	23.8-27.0	23.6 – 27.0	24.0 – 26.3
4	Disintegration Time	03minute 20 seconds	3 minutes 40 seconds	2 minutes 45 seconds
5	Friability (% w/w)	Nil	Nil	Nil
6	Thickness (mm)	5.13-5.15	5.13 – 5.16	5.12 – 5.15

From the above data, it was concluded that change in croscarmellose sodium level in studied range had no significant impact on disintegration time and dissolution profile, so concentration of croscarmellose sodium 20 mg/ tablet intragranular and 30 mg/ tablet extra granular was selected for final formulation proposed for exhibit batch

Optimization of binder level (HPC)

Table X. Physical parameters of core tablets

Batch No.		120-f04	120-F09	120-F010
Sr.No.	Parameters	Optimum Level	Lower Level (-20% w/w)	Higher Level (+20% w/w)
1	Mass of 20 tablets (mg)	15.32	15.34	15.32
2	Individual weight (mg)	765-768	763 – 768	762 – 766
3	Hardness (kp)	23.8-27.0	24.6 – 26.9	23.9 – 26.2
4	Disintegration Time	03minute 20 seconds	2 minutes 50 seconds	4 minutes
5	Friability (% w/w)	Nil	Nil	Nil
6	Thickness (mm)	5.13-5.15	5.11 – 5.18	5.13 – 5.16

From the above data, it was concluded that change in hydroxy propyl cellulose level in studied range had no significant impact on disintegration time and dissolution profile, so concentration of hydroxypropyl cellulose 10 mg / tablet was selected for final formulation proposed for exhibit batch.

Optimization of Glidant level:

Table XI. Physical parameters of core tablets

Batch No.		120-F04	120-F011	120-F012
Sr.No.	Parameters	Optimum Level	Lower Level (-20% w/w)	Higher Level (+20% w/w)
1	Mass of 20 tablets (mg)	15.32	15.31	15.32
2	Individual weight (mg)	765-768	764 – 768	760 – 769
3	Hardness (kp)	23.8-27.0	22.9 – 25.5	23.8 – 26.1
4	Disintegration Time	03minute 20 seconds	3 minutes 20 seconds	3 minutes 25 seconds
5	Friability (% w/w)	Nil	Nil	Nil
6	Thickness (mm)	5.13-5.15	5.11 – 5.16	5.13 – 5.19

From the above data, it was concluded that change in Silica colloidal anhydrous in studied range had no significant impact on uniformity of dosage units, so concentration of colloidal silicone dioxide 4 mg/ tablet was selected for final formulation proposed for exhibit batch.

Optimization of lubricant level.

Table XII. Physical parameters of core tablets

Batch No.		**120-F04**	**120-F13**	**120-F14**
Sr.No.	**Parameters**	**Optimum Level**	**Lower Level (-20% w/w)**	**Higher Level (+20% w/w)**
1	Mass of 20 tablets (mg)	15.32	15.33	15.31
2	Individual weight (mg)	765-768	765 – 769	762 – 766
3	Hardness (kp)	23.8-27.0	23.6 – 25.1	24.1 – 25.9
4	Disintegration Time	03minute 20 seconds	3 minutes 10 seconds	3 minutes 30 seconds
5	Friability (% w/w)	Nil	Nil	Nil
6	Thickness (mm)	5.13-5.15	5.14 – 5.18	5.12 – 5.16

From the above data, it was concluded that change in magnesium stearate level in studied range had no significant impact on disintegration time and dissolution profile, so concentration of magnesium stearate 4 mg/ tablet was selected for final formulation proposed for exhibit batch.

In vitro disintegration time

The internal structure of tablets that is pore size distribution, water penetration into tablets and swelling of disintegration substance are suggested to be the mechanism of disintegration. The results are shown in table 8-11 and this was determined as per I.P for all the formulations. All the formulations show disintegration time less than 4 minutes. Crospovidone has high water uptake and swelling pressure which leads to faster disintegration. Sodium starch glycolate shows disintegration time in between and Croscarmellose sodium shows more disintegration time.

In vitro dissolution Studies

All the formulations were subjected for the in vitro dissolution studies using tablet dissolution tester (USP) TDT-08L, Electro lab. Solution having pH 6.8 was used as dissolution medium. The samples were withdrawn at different time intervals, filter and analyzed. Cumulative % drug release were calculated on the basis of mean amount of febuxostat Hydrochloride present in the respective tablet. The results obtained in the In-vitro drug release for the all formulations F1 to F9 are compared. The plots are shown from figure 2, 3 and 4 for cumulative percentage drug release vs. time. The effect of Binder Glidants and Lubricants were also checked for drug release in different proportions.

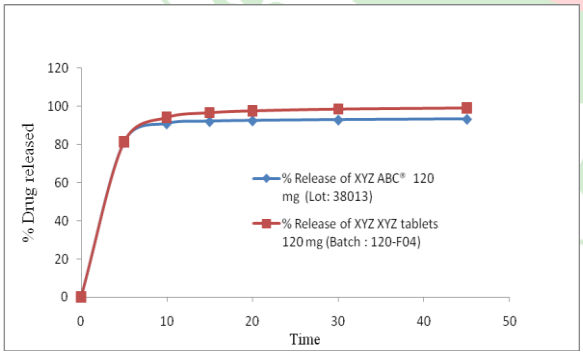

Fig. 2. Comparative dissolution profile of Marketed ® tablets, 120 mg and Febuxostat tablets 120 mg (Batch : 120-F04)

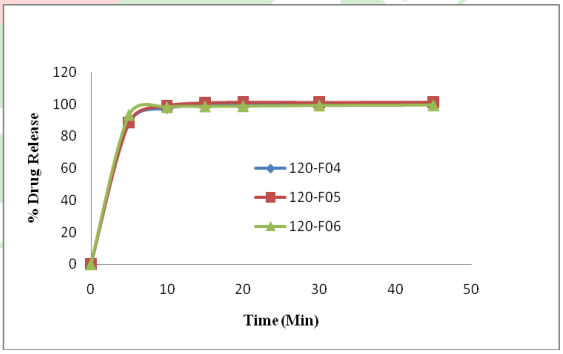

Fig. 3. Comparative dissolution profile of Febuxostat tablets 120 mg at different diluent level

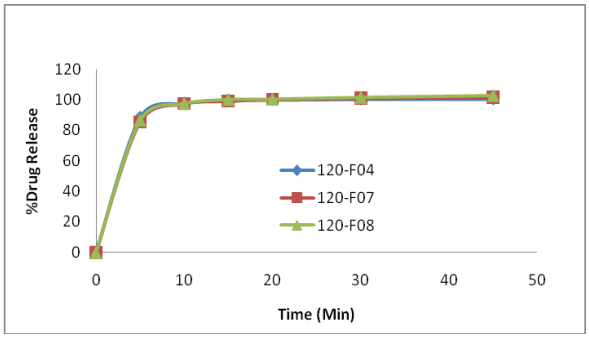

Fig. 4. Comparative dissolution profile of Febuxostat tablets 120mg at different disintegrant level

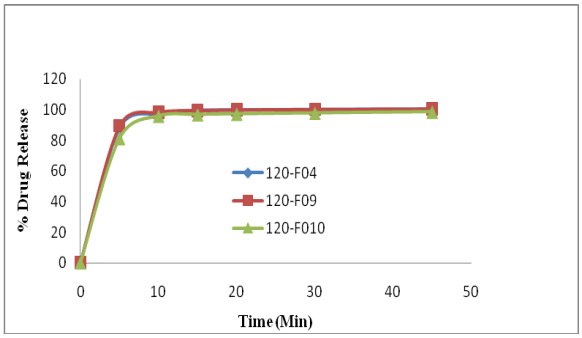

Fig. 5. Comparative dissolution profile of Febuxostat tablets 120 mg different binder level

Stability study

The accelerated stability study was carried at 40°c ±2°c/75% RH ±5% for 3 months optimized batch F04 was kept in PVC_PVC blister and Alu-Alu blisters for 3 three months for above conditions sample were analyzed.

Table 13. Stability Details of Drug with Description

Product name	**FEBUXOSTAT tablets 120 mg**					
Batch No.	**120-F04**					
Storage condition	**40°c ±2°c/75% RH ±5% RH**					
Packaging	**PVC_PVC blister**					
Test	**Specification**		**Initial 1**	**1 month**	**2 month**	**3 month**
Description	Light yellow colored, capsule shaped , film coated tablets engraved with "Z95" on one side and plain on other side.		Light yellow colored, capsule shaped , film coated tablets engraved with "Z95" on one side and plain on other side.			
Assay by HPCL	95.0% to 105.0%		98.0	98.0	100.4	99.1
Water content by KF	Not more than 8.0%		4.6	4.67	3.42	5028
Dissolution: Media : phosphate buffer pH 6.8 Volume : 900 ml Apparatus : Paddle, RPM : 50 Temp.:37°±0.5°c NLT 75% (Q) in 30 min	30 minutes	Mean	98.4	99.5	97.5	97.1
		Min	94.0	96.2	89.9	91.0
		Max	102.9	103.1	102	103.0
		%RSD	3.1	2.9	6	5.5
	45 minutes	Mean	99.0	100.9	98.4	99.2
		Min	96.0	98.0	90.9	93.5
		Max	102.5	104.5	102.3	103.5
		%RSD	2.2	2.5	5.4	4.3
Related substances						
Any individual degradation product	Not more than 0.2%		ND	ND	ND	ND
Total degradation product	Not more than 1.0%		0.03	0.04	0.04	0.04

CONCLUSION

The conclusions from the present investigation have given a suitable method based on UV-visible spectrophotometer for Febuxostat drug λmax of 235 nm in 0.01 N HCL. The Formulated IR tablet based was established by wet granulation techniques. The Optimized tablet were film coated for taste masking of unpleasant taste of Febuxostat drug to improve its patient compliance. The tablets were evaluated for pharmacopoeial and non-pharmacopoeial (industry specified) tests. Based on the results, F04 was identified as better formulation among all formulations developed for immediate release tablets.

The formulation F04 with decrease in binder quantity and increase in disintegrant quantity found suitable for the optimization process amongst all 4 trial batches. In that formulation F01 with aqueous hand granulation process with low disintegration time as compared to the reference product. F02 had decrease in disintegrating agent so higher disintegration time, F03 increases in binder quantity shows slow release at initial time point. The remaining all physical parameters of tablets were found satisfactory for formulation F04. Disintegration time and dissolution found comparable to the reference product. Uniformity of dosage units found satisfactory. Further optimization of 10 more batches with different concentration of diluents, binders, lubricant,

disintegrating agent & glidant with modification in F04 was done to check the effect of variables. The result shows no significant changes in the disintegration time, dissolution and given study profile.

The satisfactory pilot scale trials and industrial batches obtained may be ascribed to the state of immediate release of tablet for Febuxostat type of Anti Gout agent. The results suggest that such an approach may be viable to provide greater predictability in screening potential tablet formulations prior to clinical testing.

REFERENCES:

1. Kaur H. A, Review of Processing Technologies For Pharmaceutical Tablets, International Research Journal of Pharmacy, 2012;2:20-23.
2. Bhandari N, Kumar A, Choudhary A., Choudhary R., Bala R., A Review On Immediate Release Drug Delivery System, International Research Journal of Pharmaceutical and Applied Sciences, 2014,4:78-87.
3. Sahoo P.K., Delhi Institute of Pharmaceutical Sciences and Research, 2007,New Delhi.
4. Aulton M. E., "Pharmaceutics" the science of dosage form, 1988, 2nd edition churchil llivingstone.
5. Chetan P., Granulation: Preparation, Evaluation & Control 5th Annual Garnet E. Peck Symposium, 2007.
6. Prathiba T.K., Kavitha K., Selvi A., Rupesh K., Jagdeesh S., A Review on Fast Dissolving Drug Delivery Systems-A Pioneering Drug delivery Technology, Am. J. PharmTech Res., 2013, 3:4-9.
7. Kranthi Kumar K., Srinivas L., Sai Kishore V., Naseeb Basha S., Formulation and Evaluation of Poorly Soluble Febuxostat Orodispersable Tablet, American Journal of Advanced Drug Delivery, 2014;2:12-18.
8. Joseph Praveen N., Suresh Kumar J.N., Chandan Kumar B., International Journal of Research in Pharmaceutical and Nano Sciences, 2014;3:501- 508.
9. Pande V., Karale P., Goje P., Mahanavar S., An Overview on Emerging Trends in Immediate Release Tablet Technologies, Austin Therapeutics, 2016;3:12-19.