**Original Article**

# Formulation and Evaluation of Poorly Soluble Febuxostat Orodispersable Tablet

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## ABSTRACT

Febuxostat is a urate lowering drug, an inhibitor of xanthine oxidase used in the treatment of hyperuricemia and chronic gout. The drug shows dissolution-rate limited absorption, there by poor and variable bioavailability. It needs enhancement in bioavailability to derive maximum therapeutic efficacy. The main objective of the present research work is to enhance the solubility and dissolution rate of Febuxostat by preparing the Spherical agglomerates. Spherical agglomerates were prepared by the quasi emulsion solvent diffusion method. N, N-dimethyl form amide, chloroform and water were selected as good solvent, bridging liquid and poor solvents respectively. Polyethylene glycol, Poloxomer- F68 and Polyvinyl alcohol were used as a carrier. Among all the formulations prepared, spherical agglomerates prepared with Febuxostat and Poloxomer- F68 in 1:1 ratio showed highest drug release in 60 minutes. Spherical agglomerates prepared with Febuxostat and Poloxomer- F68 in 1:1 ratio was used in the preparation of orodispersible tablets. To study the influence of superdisintegrants on performance of Febuxostat Orodispersible Tablets, a set of three formulations (K1, K2, K3) were prepared using three superdisintegrants sodium starch glycolate, Croscarmalose sodium and Crospovidone . The orodispersible tablets of Febuxostat prepared with Crospovidone showed rapid drug release when compared to pure drug and other tablet formulations.

**Keywords**: Febuxostat, Poloxomer- F68, sodium starch glycolate, Croscarmalose sodium.

# INTRODUCTION[1-9]

The oral route of administration is the most important method of administering drugs for systemic effects. In this, the solid dosage form, particularly, tablets are the dosage form of a choice because of their special characteristics like unit dosage form with greatest dose precision and least content variability, lower cost, easy administration by a patient and temper proof nature. The formation of solid oral dosage forms and tablets in particular, have undergone rapid changes and development over the last several decades and one of the most revolutionary technologies in that of direct compression. It is economical, facilitates processing without the need for moisture and heat and small number of processing steps are involved. The basic requirement for commercial production of tablet is a particulate solid with good flow ability, mechanical strength and compressibility. Hence is necessary to evaluate and manipulate the above said properties. To impart these properties the drugs are subjected to particle design techniques, spherical crystallization is one the techniques of particle design. The particle size can be enhanced by the help of wet granulation method, dry granulation method, extrusion spheroinization and by spherical crystallization methods. The spherical crystallization is a nonconventional particle- size enlargement technique that involves crystallization and agglomeration using bridging liquid. Spherical crystallization is one of such particle design technique in which crystallization and agglomeration process are carried out simultaneously. Kawashima *et al*, in 1990, developed spherical crystallization technique. Spherical Crystallization process transforms the fine crystal obtains during crystallization into spherical agglomerates. Agglomerates formed further improves the flow ability and compressibility of pharmaceutical ingredient which enables direct tabletting of drug instead of further processing like mixing , granulation, sieving, drying etc. There are certain parameters which have to be optimized in order to obtain the maximum amount of spherical crystals.

## Advantages of Spherical Crystallization

- Spherical crystallization technique has been successfully utilized for improving of flow ability and compressibility of drug powder.
- This technique could enable subsequent processes such as separation, filtration, drying etc to be carried out more efficiently improved for pharmaceutical process i.e. milling, mixing and tableting because of their excellent flow ability and pack ability.
- This technique may enable crystalline forms of a drug to be converted into different polymorphic form having better bioavailability.
- For masking of the bitter taste of drug. Preparation of micro sponge, micro-spheres and nanospheres, microbaloons, nanoparticles and micro pellets as novel particulate drug delivery system.

# MATERIALS AND METHODS[10]

All the materials are listed in table no:-1.

## Methods

### Phase solubility studies of Febuxostat

Phase solubility studies were performed according to method reported by Higuchi and Connors. Excess (usually more than1mg/mL concentration) of drug was added to each 25mL of different pH Buffer solutions (pH 1.2 to 7.4), distilled water alone

and combination with 0.5%, 1%, 2% SLS taken in stopperred conical flasks and mixture were shaken for 24hrs in rotary flask shaker. After shaking to achieve equilibrium, 2ml aliquots were withdrawn at 1hr intervals and filtered through Whatman filter paper. The filtrate was diluted if necessary and analyzed by UV- spectrophotometer at 315 nm. Shaking was continued until three consecutive readings were same. Results were given in Table No:-3.

## Method used for the estimation of Febuxostat in pH 6.8 buffers

### Standard solution

Febuxostat (10mg) was dissolved in 5 ml of methanol in 10 ml volumetric flask and the solution was made up to volume with pH 6.8 buffers.

### Procedure

Calibration curve for the estimation of Febuxostat was constructed employing pH 6.8 buffer. The standard solution of Febuxostat was subsequently diluted with pH 6.8 buffer to obtain series of dilutions containing 5, 10, 15, 20 and 25μg of Febuxostat in 1.0ml of solution. The absorbance of the above solutions was measured in Elico UV Spectrophotometer at 315nm. The results are given in Table .2 and shown in Fig 1. The method obeys Beer's law in the concentration range of 5-25μg /ml. Low RSD values ensured reproducibility of the method. Thus, the method was found to be suitable for the estimation of Febuxostat content in various products and *in-vitro* dissolution studies. All the results are listed in table no:-4&Fig No:-1.

## Experimental Session

### Preparation of Spherical agglomerates

Spherical agglomerates were prepared by simple agglomeration technique.

Febuxostat (1g) was dissolved in 20 mL N, N-dimethyl formamide (good solvent) by gentle warming up to 50ºC and then cooled to room temperature. Hydrophilic polymer (Poloxamer F68 or PEG 6000 or PVP K30) in various concentrations (0.5% w/v, 0.75% w/v and 1% w/v) was dissolved in 100ml of distilled water and used as a poor solvent. The drug solution was added to the polymeric solution which was maintained with continuous stirring speed of 500 RPM. The bridging liquid Chloroform (5 mL) was added in a thin stream to drug and polymeric mixture and allowed for continuous stirring for a period of 30 minutes. The spherical crystals were collected by filteration and dried at room temperature for a period of 2 hours. The various formulations were shown in Table no.5.

## Evaluation of spherical agglomerates

### Solubility studies

The solubility of spherical agglomerates in water was determined by taking excess quantity of spherical agglomerates and adding to screw- capped 50 ml glass vials filled with water. The vials were shaken for two hours on mechanical shaker. The solution was filtered through Whatmann filter paper No.1 and the drug concentration was determined spectrophotometrically at 315 nm. All the results are listed in table no:-6

### Drug Content Estimation

The percentage drug content in spherical agglomerates was estimated by dissolving 50 mg of spherical agglomerates in methanol, mixed thoroughly by shaking and the volume was made up to the mark with pH 6.8 buffer. The solution was filtered and the filtrate was diluted suitably with pH 6.8 buffer and absorbance was measured at 315 nm using UV/Visible spectrophotometer. Results are listed in table no:-7

## Dissolution studies of agglomerates

*In-vitro* dissolution studies of pure drug and spherical agglomerates were carried out for 60 minutes using USP Dissolution test apparatus type II (Lab India DISSO 2000, eight stages) at 50 rpm. Spherical agglomerates equivalent to 20 mg of pure drug (Febuxostat) used for dissolution study at $37\pm0.5^0$ C in 900ml of pH 6.8 buffer as dissolution medium. Aliquot equal to 5 ml was withdrawn at regular time intervals (10, 20, 30, 40, 50, 60 min), an equal volume of fresh dissolution medium was replaced to maintain the sink condition and aliquots were measured at 258 nm UV/Visible spectrophotometer. $DE_{30}\%$, $T_{50}$, $T_{90}$, $k_1$ and $R^2$ values were calculated from dissolution data. Results are listed in table No:-8, 9&Fig No:-2

## Evaluation of micromeritic properties of the blend

## Bulk density

Blend was weighed and transferred to a measuring cylinder. Then bulk volume was noted. Bulk density was calculated by using the following formula

$$\text{Bulk density} = \frac{Mass\,of\,the\,powder}{Bulk\,volume}$$

## Tapped density

Blend was weighed, transferred to a measuring cylinder and subjected to 100 tapings. Then volume was noted as tapped volume. Tapped density was measured by using the following formula

$$\text{Tapped density} = \frac{Mass\,of\,the\,powder}{Tapped\,volume}$$

## Carr's index

Carr's index was calculated by using the following formula

$$\text{Carr's index} = \frac{Tapped\,density - Bulk\,density}{Tapped\,density} \times 100$$

## Hausner's ratio

Hausner's ratio was calculated by using the following formula

$$\text{Hausner's ratio} = \frac{Tapped\,density}{Bulk\,density}$$

## Angle of repose

Required quantity of blend was taken and poured into a hollow cylinder which was placed on a graph sheet. Then the cylinder was slowly lifted. Then height and diameter of the heap formed were noted down. The angle of repose ($\theta$) was calculated by the formula

$$\text{Angle of repose, } \theta = Tan^{-1}\frac{h}{r}$$

All the results are listed in table No:-10.

## Preparation of Febuxostat Orodispersible Tablets

Febuxostat containing orodispersible tablets were prepared by direct compression process. All the ingredients (shown in Table 01) were properly mixed passed through mesh no. 80. The resulting blend was lubricated with magnesium stearate and talc and compressed into tablets using the Cad mach sixteen stationary punching (round shaped, 7mm thick) machine. The various formulations were shown in Table no.11.

## Evaluation of Febuxostat Orodispersible tablets

## Weight variation test

Weight variation test was done by weighing 20 tablets individually, calculating the average weight and comparing the individual tablet weight to the average weight.

## Drug content

Twenty tablets were powdered, and 40 mg equivalent weight of Febuxostat in tablet powder was accurately weighed and transferred into a 100 ml volumetric flask. Initially, 5 ml methanol was added and shaken for 10 min. Then, the volume was made up to 100 ml with 6.8 phosphate buffer. The solution in the volumetric flask was filtered, diluted suitably and analyzed spectrophotometrically at 315 nm.

## Disintegration Time

The disintegration time was determined in distilled water at $37\pm0.5^0$ C using disintegration test apparatus USP ED-2L (Electro lab, Mumbai).

## Friability

Roche friabilator was used to determine the friability. Pre weighed tablets were placed in friabilator and rotated at a speed of 25 rpm for 4 minutes or up to 100 revolutions. The tablets are dropped from a distance of 6 inches in each revolution. The tablets were then reweighed after removal of fines and the percentage of weight loss was calculated.

%friability=Weight before friabilation – Weight after friabilation / Weight before friabilation X 100.

## Hardness

Hardness of the tablet was determined using the Monsanto hardness tester. The lower plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by tuning threaded bolts until the tablet fractured. Then the final reading was recorded. The hardness was computed by deducting the initial pressure from the final pressure.

## Wetting Time

The wetting time of the tablets can be measured using a simple procedure. Five circular tissue papers of 10 cm diameter are placed in a petridish with a 10 cm diameter. 10 mL of water-containing amaranth a water soluble dye is added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time.

## *In vitro* dispersion time

Tablet was added to 10 ml of phosphate buffer solution pH 6.8 (pH of saliva) at $37\pm0.5°C$. Time required for complete dispersion of tablet was measured.

## Fineness of dispersion

This test was performed by placing two tablets in 100 ml of water and stirring it gently, untill the tablets get completely disintegrated. Then the dispersion is passed through a sieve screen with a nominal mesh aperture of 710 μm.

All the results are listed in table No:-12.

## Dissolution studies

Dissolution studies for Febuxostat Orodispersible tablets were performed in pH 6.8 phosphate buffer using USP dissolution test apparatus (Electrolab, Mumbai, India) with a paddle stirrer. The paddles were allowed to rotate at speed of 100 rpm. The dissolution medium was maintained at a temperature of $37\pm0.5\ ^OC$ and samples were withdrawn at an interval of every 5 min the volume of the withdrawn samples were replaced by fresh dissolution medium in order to kept the volume of the dissolution medium as constant. The withdrawn samples were filtered and absorbance was measured at absorption maxima of 315nm using UV-visible spectrophotometer. All the results are listed in table No:-13&Fig No:-3.

*In-vitro* dissolution kinetic studies

The drug release data were plotted and tested with zero order (cumulative % drug released Vs time), First order (Log % remained Vs time). The in vitro dissolution kinetic parameters, dissolution rate constants (K), correlation coefficient (r), the times ($t_{50}$) for 50 % drug released (half-life) and dissolution efficiency [D.E.] were calculated. All the results are listed in table No:-14.

## CONCLUSION

The present study shows that the spherical aggumeration of Febuxostat prepared by using various polymers like poloxomer f68, PEG 6000, PVP –K30 exhibits the good micromeritic properties which are essential for direct compression and also enhances the dissolution of the drug. So this technique may apply for the production of Febuxostat Orodispersible tablets**.**

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## MATERIALS

**Table 1.** List of ingredients

| S. No | Ingredients | Supplier |
|---|---|---|
| 1 | Febuxostat | Gift sample |
| 2 | Poloxamer- F68,. | Oxford laboratory reagent, Mumbai |
| 3 | Sodium starch glycolate, | Oxford laboratory reagent, Mumbai |
| 4 | Croscarmellose sodium | Loba Chemicals, Mumbai |
| 5 | N, N-dimethyl formamide | Loba Chemicals, Mumbai |
| 6 | Chloroform | Shreeji Chemicals, Mumbai |
| 7 | Polyethylene glycol | SDFine Chemicals limited, Mumbai |
| 8 | Polyvinyl alcohol | SDFine Chemicals limited, Mumbai |
| 9 | Mannitol | SDFine Chemicals limited, Mumbai |
| 10 | Crospovidone | SDFine Chemicals limited, Mumbai |
| 11 | Methanol | Merk specialities Pvt limited, Mumbai |
| 9 | Talc | SD Fine Chemicals limited, Mumbai |
| 10 | Crospovidone | SDFine Chemicals limited |
| 11 | Avicel pH 102 | SDFine Chemicals limited |
| 12 | Mg streate | SDFine Chemicals limited |

**Table 2.** List of equipments

| S. NO | Equipments | Model and Manufacturer |
|---|---|---|
| 1 | Digital balance | Infrainstruments pvt. LTD, Chennai |
| 2 | Tablet dissolution test apparatus | Labindia DS 8000 Mumbai |
| 3 | UV-Visible spectrophotometer | Elico Ltd., SL 150, Hyderabad |
| 4 | Compression machine | Cadmach Machinery, Kolkata |
| 5 | Roche Friabilator | Campbell Electronics, Mumbai. |
| 6 | Monsanto Hardness Tester | Cadmach, Ahmedabad, India |
| 7 | Disintegration apparatus | Thermonic Campbell electronics, Mumbai |
| 8 | Digital pH meter | Digisum Electronics, Hyderabad |

**Table 3.** Phase solubility studies of febuxostat (pure drug)

| Solvent | Amount soluble ( Febuxostat ) in mg/ml |
|---|---|
| 0.1N HCl (1.2 pH) | 0.103 |
| pH 2.0 | 0.0403 |
| pH 3.0 | 0.054 |
| pH 4.5 | 0.065 |
| pH 6.8 | 0.109 |
| pH 7.4 | 0.073 |
| Distilled Water | 0.0034 |
| Distilled Water + 0.5% SLS | 0.076 |
| Distilled Water + 1% SLS | 0.084 |
| Distilled Water + 2% SLS | 0.089 |

**Table 4.** Calibration curve for the estimation of Febuxostat in pH 6.8 buffer

| Concentration (µg/ml) | Absorbance at 315nm |
|---|---|
| 0 | 0.000 |
| 5 | 0.133 |
| 10 | 0.266 |
| 15 | 0.401 |
| 20 | 0.533 |
| 25 | 0.667 |

**Table 5.** List of febuxostat spherical agglomerates formulated with different hydrophilic polymers

| Trial batches | drug (mg) | Poloxomer F68 (mg) | PEG 6000 (mg) | PVP-K30 (mg) | N,N-dimethyl Formamide (ml) | Water (ml) | Chloroform (ml) |
|---|---|---|---|---|---|---|---|
| F1 | 1000 | 500 | - | - | 20 | 100 | 5 |
| F2 | 1000 | 750 | - | - | 20 | 100 | 5 |
| F3 | 1000 | 1000 | - | - | 20 | 100 | 5 |
| F4 | 1000 | - | 500 | - | 20 | 100 | 5 |
| F5 | 1000 | - | 750 | - | 20 | 100 | 5 |
| F6 | 1000 | - | 1000 | - | 20 | 100 | 5 |
| F7 | 1000 | - | - | 500 | 20 | 100 | 5 |
| F8 | 1000 | - | - | 750 | 20 | 100 | 5 |
| F9 | 1000 | - | - | 1000 | 20 | 100 | 5 |
| F10 | 1000 | - | - | -- | 20 | 100 | 5 |
| F11 | 1000 | - | - | - | 20 | 100 | 5 |
| F12 | 1000 | - | - | - | 20 | 100 | 5 |

**Table 6.** Solubility studies of febuxostat spherical agglomerates

| Formulation | Solubility (mg/ml) |
|---|---|
| Pure drug | 0.0038 |
| FI | 0.0645 |
| F2 | 0.0762 |
| F3 | 0.0889 |
| F4 | 0.0565 |
| F5 | 0.0652 |
| F6 | 0.0773 |
| F7 | 0.0453 |
| F8 | 0.0548 |
| F9 | 0.0667 |
| F10 | 0.0342 |
| F11 | 0.0435 |
| F12 | 0.0554 |

**Table 7.** Drug content of Febuxostat spherical agglomerates

| Formulation | % of Drug content |
|---|---|
| FI | 99.18 |
| F2 | 99.23 |
| F3 | 99.63 |
| F4 | 99.44 |
| F5 | 99.14 |
| F6 | 99.27 |
| F7 | 99.12 |
| F8 | 99.71 |
| F9 | 99.19 |
| F10 | 99.25 |
| F11 | 99.37 |
| F12 | 99.16 |

**Table 8.** *In-vitro* dissolution data of Febuxostat pure drug and spherical agglomerates prepared with different polymers

| S. No | Time (min) | Cumulative % of drug release ($\overline{X}$ ± S.D.) Trial batches | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Pure drug | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
| 1 | 0 | 0. | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 10 | 2.69 | 32.36 | 36.90 | 40.22 | 29.40 | 34.11 | 37.25 | 27.30 | 32.02 | 34.28 |
| 3 | 20 | 4.80 | 39.18 | 43.74 | 47.42 | 36.37 | 40.58 | 44.41 | 34.26 | 38.48 | 42.33 |
| 4 | 30 | 6.93 | 54.75 | 59.34 | 67.04 | 51.75 | 56.34 | 60.04 | 49.63 | 54.22 | 57.92 |
| 5 | 40 | 9.76 | 72.86 | 77.47 | 81.02 | 69.84 | 74.45 | 78.06 | 67.71 | 72.32 | 75.87 |
| 6 | 50 | 11.55 | 83.03 | 88.02 | 91.41 | 80.01 | 84.98 | 88.38 | 77.86 | 82.84 | 86.23 |
| 7 | 60 | 13.09 | 90.29 | 94.61 | 97.67 | 87.59 | 91.56 | 94.26 | 85.44 | 89.41 | 92.47 |

**Table 9.** *In-vitro* dissolution kinetics of Febuxostat pure drug and spherical agglomerates prepared with different polymers

| S. No | Trial baches | Dissolution kinetics Trial batches | | | | | |
|---|---|---|---|---|---|---|---|
| | | $T_{50}$ (min) | $T_{90}$ (min) | $DE_{30}$ (%) | K (min$^{-1}$) | Zero Order | First order |
| 1 | Pure drug | 275.2 | 914.3 | 3.80 | 0.0025 | 0.9886 | 0.9902 |
| 2 | F1 | 19.8 | 65.8 | 32.98 | 0.0350 | 0.9637 | 0.9789 |
| 3 | F2 | 16.4 | 54.6 | 36.77 | 0.0422 | 0.9493 | 0.9682 |
| 4 | F3 | 13.6 | 45.3 | 39.72 | 0.293 | 0.9363 | 0.99462 |
| 5 | F4 | 21.9 | 72.7 | 30.55 | 0.0317 | 0.9724 | 0.9814 |
| 6 | F5 | 18.7 | 62.1 | 34.29 | 0.0371 | 0.9582 | 0.9774 |
| 7 | F6 | 16.3 | 54.1 | 37.24 | 0.0426 | 0.9463 | 0.9704 |
| 8 | F7 | 23.5 | 78.1 | 28.80 | 0.0295 | 0.9775 | 0.9830 |
| 9 | F8 | 20.3 | 67.3 | 32.54 | 0.0342 | 0.9643 | 0.9808 |
| 10 | F9 | 17.9 | 59.5 | 35.19 | 0.0387 | 0.9557 | 0.9770 |

**Table 10.** Micrometric properties for formulation blends

| Formulation code | Bulk density (gm/cm$^3$) | Tapped Density gm/cm$^3$) | Carr's index (%) | Hausner's ratio | Angle of repose (°) |
|---|---|---|---|---|---|
| $K_1$ | 0.453 | 0.544 | 16.72 | 1.20 | 28.63 |
| $K_2$ | 0.475 | 0.564 | 15.78 | 1.19 | 27.11 |
| $K_3$ | 0.441 | 0.517 | 14.70 | 1.18 | 25.12 |

**Table 11.** Composition of febuxostat orodispersible tablets

| Ingredients | K₁ | K₂ | K₃ |
|---|---|---|---|
| Febuxostat agglomerates | 80mg | 80 mg | 80  mg |
| Sodium Starch Glycolate(SSG) | 10 mg | - | - |
| Croscarmellose sodium | - | 10  mg | - |
| Crospovidone | - | - | 10  mg |
| Mannitol | 30 mg | 30 | 30  mg |
| Avicel pH 102 | 76  mg | 76 | 76 mg |
| Talc | 2 mg | 2 | 2  mg |
| Mg streate | 2  mg | 2 | 2  mg |
| Total weight * | 200 mg | 200 mg | 200 mg |

*Indicated one tablet weigh

**Table 12.** Evaluation parameters of febuxostat orodispersible tablets

| S. No | Parameters | K₁ | K₂ | K₃ |
|---|---|---|---|---|
| 1 | Average weight (mg) | 198±0.2 | 199±0.1 | 200±0.2 |
| 2 | Drug content (%) | 98.4 | 99.4 | 98.7 |
| 3 | Disintegration time (sec) | 153 | 144 | 124 |
| 4 | Friability (%) | 0.73 | 0.46 | 0.47 |
| 5 | Hardness (kg/sqcm) | 4.2 | 4.2 | 3.8 |
| 6 | Wetting time (sec) | 134 | 126 | 95 |
| 7 | *In-vitro* dispersion time (sec) | 258 | 213 | 163 |
| 8 | Fineness of dispersion | pass | pass | pass |

**Table 13.** Comparative *in-vitro* dissolution profile of Febuxostat Orodispersible tablet with different dispersing agents

| S. No. | Sampling time (min) | Cumulative % of drug dissolved ($\overline{X}$ ± s. d.) | | |
|---|---|---|---|---|
| | | K₁ | K₂ | K₃ |
| 1 | 0 | 0 | 0 | 0 |
| 2 | 5 | 42.14 | 43.71 | 46.77 |
| 3 | 10 | 57.38 | 59.31 | 68.94 |
| 4 | 15 | 76.55 | 78.66 | 81.88 |
| 5 | 20 | 85.70 | 89.39 | 99.00 |
| 6 | 25 | 93.15 | 98.09 | - |
| 7 | 30 | 98.54 | - | - |

**Table 14.** *In-vitro* dissolution kinetics of Febuxostat Orodispersible tablet

| S. No. | Formulation | T 50 (min) | T 90 (min) | DE 15 (%) | K (min$^{-1}$) | Correlation coefficient values | |
|--------|-------------|------------|------------|-----------|----------------|-------------|-------------|
|        |             |            |            |           |                | Zero Order | First order |
| 1 | K$_1$ | 5.9 | 19.7 | 45.93 | 0.116 | 0.8839 | 0.9618 |
| 2 | K$_2$ | 5.3 | 17.7 | 47.45 | 0.137 | 0.9212 | 0.9511 |
| 3 | K$_3$ | 4.7 | 15.6 | 52.89 | 0.147 | 0.9250 | 0.9521 |
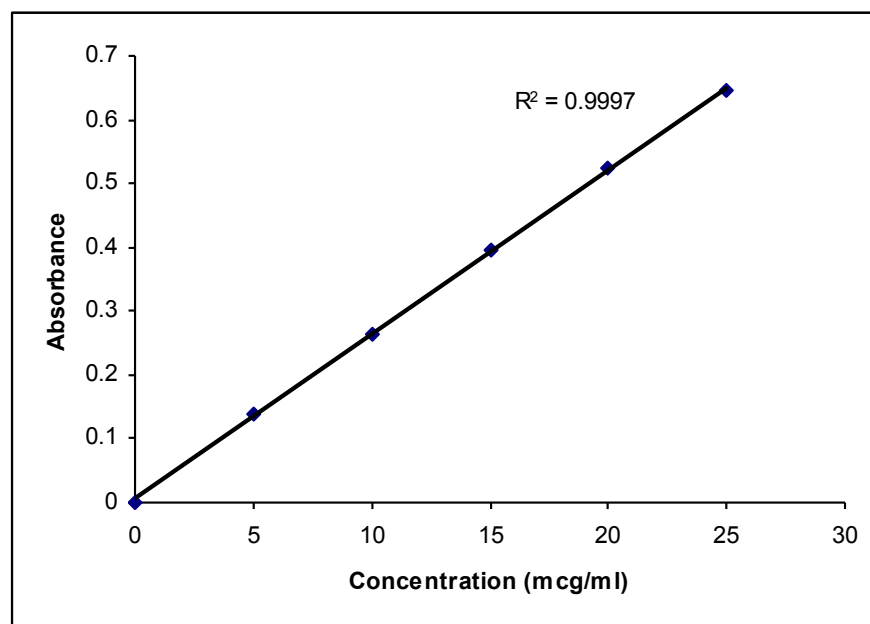


**Figure 1.** Calibration curve for the estimation of Febuxostat in  pH 6.8 buffer