PHARMACEUTICAL COMPOSITON OF FEBUXOSTAT

ABSTRACT

The present invention relates to a stable and improved pharmaceutical composition of febuxostat or salts thereof, its process of manufacturing and use in the treatment of chronic hyperuricemia in gout patient.

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We claim:

1. A pharmaceutical composition comprising febuxostat or salt thereof, at least one solubility enhancing agent, and one or more pharmaceutically acceptable excipients.

2. The pharmaceutical composition of claim 1, wherein the solubility enhancing agent comprises one or more of surfactants, hydrocolloids and polymers.

3. The pharmaceutical composition of claim 2, wherein the solubility enhancing agent comprises one or more of sodium lauryl sulphate, hydroxypropyl methyl cellulose, hydroxypropyl cellulose, hydroxyl methyl cellulose, N-vinyl-2-pyrrolidone, polyvinyl pyrrolidone, and vinylpyrrolidone - vinylacetate copolymer.

4. The pharmaceutical composition of claim 1, wherein the composition comprises about 0.01% to about 30 % w/w of solubility enhancing agent.

5. The pharmaceutical composition of claim 1, wherein the ratio of amount of febuxostat or its salt to the amount of solubility enhancing agent is in the range of about 1:0.01 to about 1:2.

6. The pharmaceutical composition of claim 1, wherein the average particle diameter of febuxostat or salt thereof is in the range of about 1 micron to less than about 12 micron.

7. The pharmaceutical composition of claim 1, wherein the average particle diameter of febuxostat or salt thereof is about 10 micron.

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8. A pharmaceutical composition comprising –

(a) about 20mg to about 100 mg of febuxostat or salt thereof;

(b) about 80mg to about 170mg of microcrystalline cellulose;

(c) about 200mg to about 325mg of lactose;

(d) about 5mg to about 20mg of polyvinyl pyrrolidone;

(e) about 15mg to about 30mg of croscarmellose sodium; and

(f) about 1mg to about 15mg of colloidal silicon dioxide and/or sodium stearyl fumarate,

wherein the average particle diameter of febuxostat or salt thereof is in the range of about 1 micron to less than about 12 micron.

9. A process for preparing a pharmaceutical composition of febuxostat or salt thereof, the process comprising-

(a) granulating febuxostat or salt thereof with one or more solubility enhancing agent, and optionally with one or more pharmaceutically acceptable excipients; and

(b) formulating the granules in to suitable dosage form.

10. A process of preparing the pharmaceutical composition of claim 1, the process comprising the steps of:

(a) preparing granules comprising febuxostat or salt thereof, one or more solubility enhancing agents, one or more disintegrants, and optionally one or more pharmaceutically acceptable excipients;

(b) mixing granules prepared in step (a) with one or more disintegrants and lubricants; and

(c) formulating the mixture prepared in step (b) in to suitable dosage form.

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Dated this 9th day of July, 2011

Signature:

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PHARMACEUTICAL COMPOSITION OF FEBUXOSTAT

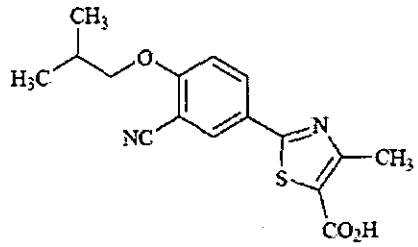
FIELD OF THE INVENTION

The present invention relates to pharmaceutical composition of febuxostat or salt thereof for oral administration. More particularly, it relates to a stable and improved pharmaceutical composition of febuxostat or salt thereof, and process of producing the same.

BACKGROUND OF THE INVENTION

Febuxostat has a strong activity for inhibiting xanthine oxidase or a uric acid decreasing action, and it is indicated for use in the treatment of gout or hyperuricemia.

Chemically, febuxostat is (2-(3-cyano-4-isobutyloxyphenyl)-4-methyl-5-thiazolecarboxylic acid), having below structure-



Tablets of febuxostat for oral administration are currently being marketed in United States under the name ULORIC® by Takeda, and are available in two dosage strengths, 40 mg and 80 mg. Inactive ingredients include lactose monohydrate, microcrystalline cellulose, hydroxypropyl cellulose, sodium croscarmellose, silicon dioxide and magnesium stearate.

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International (PCT) Publication No. WO92/09279 discloses 2-(3-cyano-4-isobutyloxyphenyl)-4-methyl-5-thiazolecarboxylic acid (Febuxostat) has a strong activity for inhibiting xanthine oxidase or a uric acid decreasing action, and it is expected to be a therapeutic agent for gout or hyperuricemia.

International (PCT) Publication No. WO 99/65885 discloses various crystalline polymorphs of febuxostat viz., crystal form A, crystal form B, crystal form C, crystal form D, & crystal form G; and an amorphous, also referred to as crystal form E. The publication also describes that crystals A, C and G are useful in view of retention of a crystal form in long term storage. Among them, crystal A is preferred in view of industrial superiority.

U.S. Patent No. 5,614,542 discloses methods of making xanthine oxidoreductase inhibiting compounds including febuxostat.

U.S. Patent No. 7,361,676 discloses solid oral dosage form of febuxostat crystal form A.

It is known that crystal form A, C, and G of febuxostat are preferred for formulation development and crystal form A being most suitable. However, in formulating febuxostat, it is difficult to obtain preparations having less or no variation in the dissolution profiles of drugs, even if such preferred crystal forms are used as they are thought to be most stable in a physical stability test.

Thus, there exists a need to develop stable pharmaceutical compositions of febuxostat which can accommodate its all known crystalline and amorphous forms without compromising on the formulation properties as well as dissolution profile of the formulation.

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SUMMARY OF THE INVENTION

In one general aspect, there is provided a pharmaceutical composition comprising febuxostat or salt thereof, at least one solubility enhancing agent, and one or more pharmaceutically acceptable excipients.

In another general aspect, there is provided a pharmaceutical composition comprising febuxostat or salt thereof, at least one solubility enhancing agent, and one or more pharmaceutically acceptable excipients, wherein the amount of solubility enhancing agent ranges from about 0.01 to about 30 % w/w of the composition.

In another general aspect, there is provided a pharmaceutical composition comprising febuxostat or salt thereof, at least one solubility enhancing agent , and one or more pharmaceutically acceptable excipients, wherein the ratio of amount of febuxostat or its salt to the amount of solubility enhancing agent is in the range of about 1:0.01 to about 1:2.

In another general aspect, there is provided pharmaceutical composition comprising febuxostat or salt thereof, at least one solubility enhancing agent, and one or more pharmaceutically acceptable excipients, wherein the average particle diameter of febuxostat or salt thereof ranges from about 1 micron to less than about 12 micron.

In another general aspect, there is provided a pharmaceutical composition comprising febuxostat or salt thereof, at least one solubility enhancing agent, and one or more pharmaceutically acceptable excipients, wherein the average particle diameter of febuxostat or salt thereof is about 10 micron.

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In another general aspect, there is provided pharmaceutical composition comprising febuxostat or salt thereof, at least one solubility enhancing agent, and one or more pharmaceutically acceptable excipients, wherein said composition retains at least 80% of potency of febuxostat or salt thereof after storage for three months at 40°C and 75% relative humidity.

In another general aspect, there is provided pharmaceutical composition comprising febuxostat or salt thereof, at least one solubility enhancing agent, and one or more pharmaceutically acceptable excipients, wherein said composition exhibits no significant difference in rate and/or extent of absorption of febuxostat or salt thereof as compared to marketed formulation of febuxostat available under the trade name ULORIC®.

Embodiments of the pharmaceutical composition may include one or more of the following features. For example, the pharmaceutical composition may include one or more pharmaceutically acceptable excipients selected from binders, fillers, lubricants, disintegrants, glidants, antioxidants, solvents, flavors, sweeteners and the like.

In another general aspect, there is provided a process of preparing pharmaceutical composition of febuxostat or salt thereof, which process comprises mixing and/or granulating febuxostat or salts thereof and at least one solubility enhancing agent with one or more pharmaceutically acceptable excipients.

In another general aspect, there is provided a process of preparing pharmaceutical composition of febuxostat or salt thereof, which process comprises step of granulating febuxostat or salt thereof with one or more

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pharmaceutically acceptable excipients followed by partial or complete coating of said granules with one or more solubility enhancing agent.

Embodiments of the pharmaceutical composition may include one or more of the following features. For example, the pharmaceutical composition may include one or more pharmaceutically acceptable excipients selected from binders, fillers, lubricants, disintegrants, glidants, antioxidants, solvents, flavors, sweeteners and the like.

In another general aspect, there is provided a method of treating or managing chronic hyperuricemia in patient with gout comprising administering to said subject a pharmaceutical composition of febuxostat or salt thereof comprising at least one solubility enhancing agent and one or more pharmaceutically acceptable excipients.

In another general aspect, there is provided a method of treating or managing asymptomic hyperuricemia in patient comprising administering to said subject a pharmaceutical composition comprising febuxostat or salt thereof, at least one solubility enhancing agent, and one or more pharmaceutically acceptable excipients.

The details of one or more embodiments of the invention are set forth in the description below. Other features, objects and advantages of the invention will be apparent from the description.

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DETAILED DESCRIPTION OF THE INVENTION

The inventors of the present invention have developed a stable formulation of febuxostat which demonstrates little or no variation in the dissolution profile.

In particular, the present inventors have surprisingly found that when solubility enhancing agent is used in formulating the composition of febuxostat or its salt irrespective of its crystal characteristics; the resulting formulation demonstrates suitable dissolution profile which is ideal for oral delivery. Moreover the formulation also found to remain physico-chemically stable as well as possessing improved formulation characteristics.

Thus, there is provided a pharmaceutical composition of febuxostat or its salt comprising at least one solubility enhancing agent and one or more pharmaceutically acceptable excipients.

The terms "febuxostat" is used in broad sense to include not only the febuxostat *per se* but also its pharmaceutically acceptable salts, pharmaceutically acceptable solvates, pharmaceutically acceptable hydrates, pharmaceutically acceptable enantiomers, pharmaceutically acceptable derivatives, pharmaceutically acceptable polymorphs and pharmaceutically acceptable prodrugs.

Various crystalline forms of febuxostat or its salt may be employed in the pharmaceutical composition of the present invention. Examples of crystalline forms febuxostat include, but not limited to crystal form A, crystal form B, crystal form C, crystal form D, crystal form G; or amorphous from.

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The term "solubility enhancing agent" used throughout the description to include surfactants; hydrocolloids such as cellulose derivatives (e.g. hydroxypropyl methyl cellulose, hydroxypropyl cellulose, hydroxyl methyl cellulose); polymers such as N-vinyl-2-pyrrolidone, polyvinyl pyrrolidone; copolymers such as copolymer of vinylpyrrolidone (VP) and vinylacetate (VA). Preferably, solubility enhancing agent used in the pharmaceutical composition of febuxostat is surfactant, polyvinyl pyrrolidone or combination thereof.

Suitable "surfactants" which can be used for preparing pharmaceutical composition of febuxostat may include one or more of anionic, cationic, non-ionic or zwitterionic surfactants or mixtures thereof.

Suitable cationic surfactants may include one or more of quaternary ammonium compounds, such as benzalkonium chloride, cetyl trimethyl ammonium bromide and dodecyl dimethyl ammonium bromide, hexadecyl (cetyl) trimethylammonium bromide, dodecyl pyridinium chloride, lauryl dimethyl benzyl ammonium chloride, acyl carnitine hydrochlorides, alkyl pyridinium halides, dodecylamine hydrochloride and the like.

Suitable anionic surfactants may include one or more of salts of aliphatic monoesters of sulfuric acid and soaps, such as potassium laurate; sodium dodecyl sulphate; alkyl polyoxyethylene sulfates; sodium alginates; sodium lauryl sulphate and sodium heptadecyl sulphate; sulfonated aromatic agents such as alkyl benzene sulfonic acids and salts thereof, such as tridecylbenzene sulphonic acid and the sodium and amino salts of dodecylbenzene sulphonic acid; alkyl naphthalene sulfonates, such as sodium butylnaphthalene sulphonate, sulphosuccinates such as sodium dioctyl sulphosuccinate and N-acyl-N-alkyl fatty acid taurates; sulfated polyoxyethylated alcohols; sulfated oils; dioctyl sodium sulfosuccinate,

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phosphatidyl choline, phosphatidyl glycerol, phosphatidyl inosine, phosphatidylserine, phosphatidic acid and their salts, glyceryl esters, sodium carboxymethylcellulose, cholic acid and other bile acids (e.g., cholic acid, deoxycholic acid, glycocholic acid, taurocholic acid, glycodeoxycholic acid) or salts thereof, and the like. The preferred anionic surfactant for use in febuxostat composition is sodium lauryl sulphate.

Suitable non-ionic surfactants may include one or more of polyoxyethylene fatty alcohol ethers (Macrogol and Brij), polyoxyethylene sorbitan fatty acid esters (Polysorbates), polyoxyethylene fatty acid esters (Myrj), sorbitan esters (Span), glycerol monostearate, polyethylene glycols, polypropylene glycols, cetyl alcohol, cetostearyl alcohol, stearyl alcohol, aryl alkyl polyether alcohols, polyoxyethylene-polyoxypropylene copolymers (poloxomers), polaxamines, methylcellulose, hydroxycellulose, hydroxy propylcellulose, hydroxy propylmethylcellulose, noncrystalline cellulose, polyvinyl alcohol, polyvinylpyrrolidone, and the like.

In a preferred form of the invention the nonionic surfactant is a polyoxyethylene and polyoxypropylene copolymer and preferably a block copolymer of propylene glycol and ethylene glycol. Such polymers are sold under the tradename Poloxamer also sometimes referred to as Pluronic. Among polyoxyethylene fatty acid esters is included those having short alkyl chains. One example of such a surfactant is Solutol®. HS 15, polyethylene-660-hydroxystearate and the like.

Suitable zwitterionic surfactants may include one or more of alkyl betaines, alkyl amidopropyl betaines, alkyl sulphobetaines, alkyl glycinates, alkyl carboxyglycinates, alkyl amphopropionates, alkyl amidopropyl hydroxysultaines, acyl taurates and acyl glutamates wherein the alkyl and acyl

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groups have from 8 to 18 carbon atoms such as cocamidopropyl betaine, *sodium cocoamphoacetate, cocamidopropyl hydroxysultaine, sodium* cocamphopropionate,.and the like.

Advantageously, the solubility enhancing agents in the composition have been found to enhance the wettability and thus, the speed, extent of release and/or absorption of febuxostat or its salt, from the composition. The amount of solubility enhancing agent in the pharmaceutical composition ranges from about 0.01% to about 30% w/w of the composition.

The average diameter of febuxostat particles in the composition of the present invention may range from about 1 micron to less than about 12 micron, more preferably, the average particle diameter of febuxostat particles is about 10 microns.

It was also found that the composition comprising febuxostat particles of any known crystalline form of febuxostat having average particle diameter in the said range, the resulting composition may exhibit excellent formulation characteristics (e.g. content uniformity, disintegration time, and friability) and consistent dissolution profile.

In an embodiment, the composition of the present invention exhibits no significant difference in rate and/or extent of absorption of febuxostat or salt thereof as compared to marketed formulation of febuxostat available under the trade name ULORIC®.

The pharmaceutical composition of febuxostat may be developed in the form of powders, pellets, granules, microspheres, minitablets or any suitable solid unit forms known to person skilled in the art which can be incorporated in

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capsules or sachets; mouth dissolving tablets; dispersible tablets; effervescent tablets; multilayer tablet; inlay tablet. The preferred dosage forms are tablets and capsules filled with pellets, granules or mintablets as these are more convenient and easier to administer.

The pharmaceutical composition of febuxostat can be manufactured by using various granulation techniques known to the person skilled in the art, such as, but not limited to direct compression, wet granulation, dry granulation, hot melt granulation, hot melt extrusion, fluidized bed granulation, extrusion, and solvent evaporation.

The components of the pharmaceutical composition defined hereinbefore can be brought together into a suitable composition for oral administration according to standard practice and procedures well known in the art of pharmaceutical science using conventional formulation and manufacturing techniques.

In one embodiment, febuxostat composition may be prepared by granulating the admixture of febuxostat or its salt and solubility enhancing agent optionally with one or more pharmaceutical excipients. The resulting granules may be compressed to form tablets or filled in hard gelatin capsules.

Alternatively, the process of manufacturing the febuxostat composition may comprise a step of granulating febuxostat or its salt with one or more pharmaceutical excipients followed by complete or partial coating of the resulting granules with solubility enhancing agent. The coated granules may be compressed to form tablets or filled in hard gelatin capsules.

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In another embodiment, febuxostat composition may be developed in the form of pellets, which can be prepared by coating one or more layers of febuxostat or its salt and solubility enhancing agent on non-pareil sugar seeds or inert core (e.g. lactose beads).

Alternatively, the pellets can be prepared by completely or partially coating particles of febuxostat or its salt by solubility enhancing agent. The resulting pellets may be admixed with pharmaceutical excipients and filled into hard gelatin capsules or may be compressed with pharmaceutical excipients to form tablets.

The composition may be seal coated. Preferably, the composition is seal coated and finally film coated. The composition can be coated with ready color mix systems (such as Opadry color mix systems).

In a further embodiment, the process of manufacturing the febuxostat composition may comprise granulating febuxostat with a first quantity of disintegrant, admixing resulting granules with a second quantity of disintegrant, and formulating the resulting admixture into suitable dosage form.

In yet another embodiment, the pharmaceutical composition may involve one or more manufacturing process to obtain a single unitary dosage form i.e. wherein the or each drug is processed by granulation techniques as discussed above and finally compacted to yield a single dosage form.

Pharmaceutically acceptable excipients for use in the pharmaceutical composition comprise one or more diluents, bulking agents, binders, disintegrants, glidants, lubricants, sweeteners/taste masking agents, compression aids, colorants and flavors.

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Suitable diluents or bulking agents which includes, but are not limited to, saccharides, including monosaccharides, disaccharides, polysaccharides and sugar alcohols such as arabinose, lactose, dextrose, sucrose, fructose, maltose, mannitol, erythritol, sorbitol, xylitol lactitol, and other bulking agents such as powdered cellulose, microcrystalline cellulose (e.g. MCC PH 101 and MCC PH 102), purified sugar and derivatives thereof. The formulation may incorporate one or more of the above bulking agents, preferably, lactose & microcrystalline cellulose forms the bulking agent.

Suitable binders or binders, which includes, but are not limited to, methyl cellulose, hydroxypropyl cellulose (HPC), hydroxypropyl methyl cellulose (HPMC), starch, gelatin, gum Arabic, ethyl cellulose, polyvinyl alcohol, tragacanth, sodium alginate and equivalents thereof.

Suitable disintegrants which includes, but are not limited to, croscarmellose sodium, crospovidone, sodium starch glycolate, corn starch, potato starch, maize starch and modified starches, calcium silicates, low substituted hydroxy-propylcellulose. Preferably, disintegrant employed in the febuxostat composition is croscarmellose sodium.

Suitable lubricants and glidants which may include, but are not limited to, stearic acid and its derivatives or esters like sodium stearate, magnesium stearate and calcium stearate and the corresponding esters such as sodium stearyl fumarate; talc and colloidal silicon dioxide respectively.

Suitable taste masking agents may include one or more of polymers, sweeteners and flavors. Most preferred polymers include one or more of cellulose acetate, polymethacrylates, hydroxypropylmethyl cellulose,

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hydroxypropyl cellulose, hydroxylethyl cellulose; and the like. Most preferred sweeteners include but not limiting to one or more of aspartame, saccharin, sucralose, glycyrrhizin; and the like.

Suitable sweeteners that may be used, comprises saccharides such as sucrose, dextrose, glucose, maltose, dextrins, D-tagatose, trehalose, dried invert sugar, fructose, levulose, galactose, corn syrup solids, and the like, alone or in combination. Other examples of sweeteners comprise sodium saccharin; aspartame; sugarless sweeteners including polyhydric alcohols such as sorbitol, mannitol, xylitol, glycerol, hydrogenated starch hydrolysates, maltitol, isomaltitol, erythritol, lactitol and the like, alone or in combination.

Suitable flavors that may be used, comprise cinnamon, wintergreen, eucalyptus, spearmint, peppermint, menthol, anise as well as fruit flavors such as apple, pear, peach, strawberry, cherry, apricot, orange, watermelon, banana and the like; bean-derived flavors, such as coffee, cocoa and the like or mixtures thereof.

The invention further provides a method of treating or managing chronic hyperuricemia or asymptomic hyperuricemia in patient with gout comprising administering to said subject a pharmaceutical composition of febuxostat as substantially disclosed hereinbefore.

The invention is further illustrated by the following examples which are provided to be exemplary of the invention and do not limit the scope of the invention. While the present invention has been described in terms of its specific embodiments, certain modifications and equivalents will be apparent to those skilled in the art and are intended to be included within the scope of the present invention.

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Example 1:

Table 1

Sr. No.	Ingredients	Qty (mg/tablet)
1	Febuxostat	80.00
2	Microcrystalline cellulose	246.00
3	Lactose monohydrate	100.00
4	Polyvinyl pyrrolidone	8.00
5	Croscarmellose sodium	50.00
6	Sodium lauryl sulphate	10.00
7	Silicon dioxide	3.00
8	Magnesium stearate	3.00
9	Water	q. s.
	Total	500

Process: Febuxostat, microcrystalline cellulose and lactose monohydrate were granulated and coated with polyvinyl pyrrolidone and sodium lauryl sulphate. The granules were then mixed with croscarmellose sodium, silicon dioxide and magnesium stearate to obtain lubricated granules which were then compressed to form tablets.

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Example 2:

Table 2

Sr. No.	Ingredients	Qty (mg/tablet)
1	Febuxostat	80.00
2	Microcrystalline cellulose PH 101	135.00
3	*Lactose monohydrate*	282.00
4	Polyvinyl pyrrolidone	12.00
5	Croscarmellose sodium	25.00
6	Colloidal Silicon dioxide	6.00
7	Sodium stearyl fumarate	10.00
8	Water	Q. S.
	Total	550

Process: Febuxostat, microcrystalline cellulose, lactose monohydrate and croscarmellose sodium were granulated and coated with polyvinyl pyrrolidone. The granules were then mixed with colloidal silicon dioxide and sodium stearyl fumarate to obtain lubricated granules which were then compressed to form tablets.

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Example 3:

Table 3

Sr. No.	Ingredients	Qty (mg/tablet)
1	Febuxostat	80.00
2	Microcrystalline cellulose PH 102	135.00
3	Lactose monohydrate	282.00
4	Polyvinyl pyrrolidone	12.00
5	Croscarmellose sodium	25.00
6	Colloidal Silicon dioxide	6.00
7	Sodium stearyl fumarate	10.00
8	Water	Q. S.
	Total	550

Process: Febuxostat, microcrystalline cellulose, lactose monohydrate and part quantity of croscarmellose sodium were granulated and coated with polyvinyl pyrrolidone. The granules were then mixed with croscarmellose sodium (remaining quantity), colloidal silicon dioxide and sodium stearyl fumarate to obtain lubricated granules which were then compressed to form tablets.

Example 4: Dissolution study

Table 4 provides dissolution data of febuxostat tablet prepared as per Example 2, 3 and reference formulation (ULORIC® Tablet). For determination of drug release rate, USP Type II (Paddle) apparatus (50rpm) was used wherein 900ml of Potassium Phosphate buffer of pH 6.2 was used as medium.

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Table 4

Time (min)	Reference (% Drug Release)	Example 2 (% Drug Release)	Example 3 (% Drug Release)
0	0	0	0
5	76.0	69.6	86.7
10	83.8	78.9	97.1
15	86.4	84.2	99.1
20	88.3	89.1	99.8
30	89.1	93.6	100.2
45	89.9	96.8	100.5
60	90.5	97.2	100.6

Table 5 provides dissolution data of febuxostat tablet prepared as per Example 2, 3 and reference formulation (ULORIC® Tablet). For determination of drug release rate, USP Type II (Paddle) apparatus (75rpm) was used wherein 900ml of 0.05M Potassium Phosphate buffer of pH 6.8 was used as medium.

Table 5

Time (min)	Reference (% Drug Release)	Example 2 (% Drug Release)	Example 3 (% Drug Release)
0	0	0	0
5	95.8	97.9	98.5
10	103.2	100.5	100.7
15	103.1	99.7	100.2
20	103.5	99.3	100.0
30	102.2	100.5	100.5

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Table 6 provides dissolution data of febuxostat tablet prepared as per Example 2, 3 and reference formulation (ULORIC® Tablet). For determination of drug release rate, USP Type II (Paddle) apparatus (50rpm) was used wherein 900ml of Phosphate buffer of pH 5.5 was used as medium.

Table 6

Time (min)	Reference (% Drug Release)	Example 2 (% Drug Release)	Example 3 (% Drug Release)
0	0	0	0
5	31.5	32.6	40.7
10	41.1	39.8	49.1
15	47.9	44.2	53.4
20	52.8	47.1	54.8
30	57.0	51.2	57.6
45	60.2	54.7	60.3
60	63.3	56.7	62.2

Example 5: Stability study

Table 7

	Example 2		Example 3	
Impurity	**Initial**	**2 weeks**	**Initial**	**2 weeks**
Acid amide impurity	0.11	0.11	0.11	0.11
RRT 0.41	BQL	BQL	BQL	BQL
RRT 0.75	BQL	BQL	BQL	BQL
Total Impurities	0.11	0.11	0.11	0.11
Assay	97.6	98.3	100.6	100.0

BQL: Below Quantitation Limit

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Table 7 provides stability data of the composition of the invention when stored at 40°C and 75% relative humidity for two weeks and indicates that the composition remains stable over the storage period.

While the invention has been described in terms of its specific embodiments, certain modifications and equivalents will be apparent to those skilled in the art and are intended to be included within the scope of the invention.

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We claim:

1. A pharmaceutical composition comprising febuxostat or salt thereof, at least one solubility enhancing agent, and one or more pharmaceutically acceptable excipients.

2. The pharmaceutical composition of claim 1, wherein the solubility enhancing agent comprises one or more of surfactants, hydrocolloids and polymers.

3. The pharmaceutical composition of claim 2, wherein the solubility enhancing agent comprises one or more of sodium lauryl sulphate, hydroxypropyl methyl cellulose, hydroxypropyl cellulose, hydroxyl methyl cellulose, N-vinyl-2-pyrrolidone, polyvinyl pyrrolidone, and vinylpyrrolidone - vinylacetate copolymer.

4. The pharmaceutical composition of claim 1, wherein the composition comprises about 0.01% to about 30 % w/w of solubility enhancing agent.

5. The pharmaceutical composition of claim 1, wherein the ratio of amount of febuxostat or its salt to the amount of solubility enhancing agent is in the range of about 1:0.01 to about 1:2.

6. The pharmaceutical composition of claim 1, wherein the average particle diameter of febuxostat or salt thereof is in the range of about 1 micron to less than about 12 micron.

7. The pharmaceutical composition of claim 1, wherein the average particle diameter of febuxostat or salt thereof is about 10 micron.

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8. A pharmaceutical composition comprising –

(a) about 20mg to about 100 mg of febuxostat or salt thereof;

(b) about 80mg to about 170mg of microcrystalline cellulose;

(c) about 200mg to about 325mg of lactose;

(d) about 5mg to about 20mg of polyvinyl pyrrolidone;

(e) about 15mg to about 30mg of croscarmellose sodium; and

(f) about 1mg to about 15mg of colloidal silicon dioxide and/or sodium stearyl fumarate,

wherein the average particle diameter of febuxostat or salt thereof is in the range of about 1 micron to less than about 12 micron.

9. A process for preparing a pharmaceutical composition of febuxostat or salt thereof, the process comprising-

(a) granulating febuxostat or salt thereof with one or more solubility enhancing agent, and optionally with one or more pharmaceutically acceptable excipients; and

(b) formulating the granules in to suitable dosage form.

10. A process of preparing the pharmaceutical composition of claim 1, the process comprising the steps of:

(a) preparing granules comprising febuxostat or salt thereof, one or more solubility enhancing agents, one or more disintegrants, and optionally one or more pharmaceutically acceptable excipients;

(b) mixing granules prepared in step (a) with one or more disintegrants and lubricants; and

(c) formulating the mixture prepared in step (b) in to suitable dosage form.

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