Abstract

The invention relates to solid pharmaceutical composition comprising Rivaroxaban, or a pharmaceutically acceptable salt thereof and at least one pharmaceutically acceptable excipient. The invention also relates to a process for the preparation of a solid pharmaceutical composition comprising Rivaroxaban, or a pharmaceutically acceptable salt thereof, the process comprising (a) providing a mixture comprising Rivaroxaban and at least one pharmaceutically acceptable excipient and (b) converting said mixture to a solid pharmaceutical composition.

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We claim:

1. A solid oral dosage form comprising:
   a) Co-milled fraction of Rivaroxaban and surfactant;
   b) Inert granules comprising a hydrophilic polymer, and one or more pharmaceutically acceptable excipient(s);

   wherein, said inert granules are free of Rivaroxaban.
2. The solid oral dosage form according to claim 1, wherein surfactant is selected from sodium lauryl sulfate, polyoxyehtylene polyoxypropylene glycol, polyethylene glycol, polyoxyehtylene glycol and ethers, polysorbates, glycerol and sorbitan esters.
3. The solid oral dosage form according to claim 2, wherein surfactant is sodium lauryl sulfate.
4. The solid oral dosage form according to claim 1, wherein said pharmaceutically acceptable excipient(s) is selected from filler, binder, surfactant, disintegrant and lubricant.
5. The solid oral dosage form according claim 1, wherein hydrophilic polymer is selected from hydroxypropylcellulose, hydroxypropylmethylcellulose, hydroxyethylcellulose, polyvinylpyrrolidone, polyvinyl alcohols, polyethylene glycol and propylene glycol.
6. The solid oral dosage form according claim 5, wherein hydrophilic polymer is hydroxypropylmethylcellulose.
7. A solid oral dosage form comprising rivaroxaban or pharmaceutically acceptable salt thereof prepared by process comprising:
   a) Preparation of inert granules comprising a hydrophilic polymer and one or more pharmaceutically acceptable excipient(s), by aqueous granulation.
   b) Co-milling Rivaroxaban, a surfactant and optionally one or more pharmaceutically acceptable excipient(s).
   c) Adding co-milled fraction of Rivaroxaban prepared in step (b) with said inert granules prepared in step (a).

d) Optionally adding one or more pharmaceutically acceptable excipient(s) with said mixture/blend prepared in step (c).

e) Compressing the resultant mixture/blend of step (c) or (d) into tablets.

8. The solid oral dosage form comprising rivaroxaban or pharmaceutically acceptable salt thereof prepared according to claim 7 comprising:

a) Preparation of inert granules comprising a hydroxypropylmethylcellulose, lactose, microcrystalline cellulose, sodium lauryl sulfate and croscarmellose sodium by aqueous granulation and then drying.

b) Co-milling Rivaroxaban and sodium lauryl sulfate.

c) Adding co-milled fraction of Rivaroxaban prepared in step (b) with said inert granules prepared in step (a), by dry-mixing.

d) Adding microcrystalline cellulose, croscarmellose sodium and magnesium stearate with said mixture/blend prepared in step (c).

e) Compressing the resultant mixture/blend of step (d) into tablets.

9. A solid pharmaceutical composition, as herein described with reference to the examples accompanying the specification.

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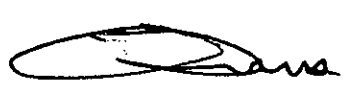

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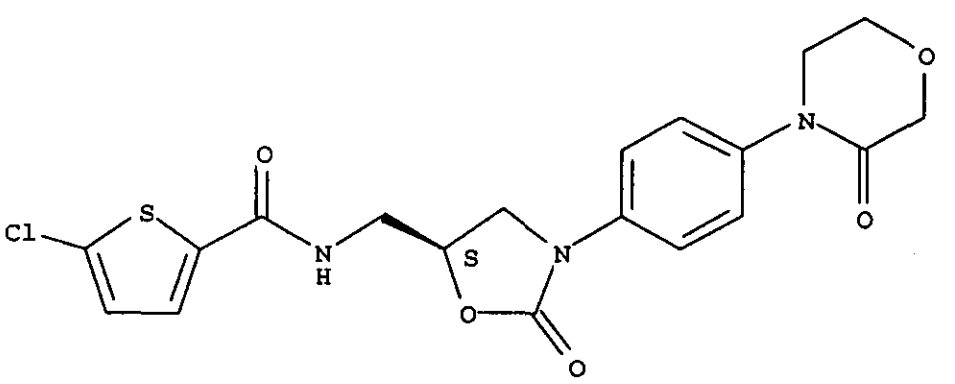
Pharmaceutical composition of Rivaroxaban

FIELD OF INVENTION

The present invention relates to a solid oral dosage form comprising (a) Rivaroxaban and (b) inert granules comprising a hydrophilic polymer, and one or more pharmaceutically acceptable excipient(s), wherein said inert granules are free of Rivaroxaban. The present invention also relates to a solid oral dosage form comprising inert granules obtainable by granulating a hydrophilic polymer, and one or more pharmaceutically acceptable excipient(s) and adding Rivaroxaban and optionally one or more pharmaceutically acceptable excipients with said inert granules.

BACKGROUND

Rivaroxaban (Formula-I), is a low molecular weight, orally administrable inhibitor of blood clotting factor Xa, which can be employed for the prophylaxis and/or treatment of various thromboembolic diseases. It is available commercially in US and Europe as Xarelto® 10, 15 & 20 mg oral immediate release tablet.



Formula-I

Rivaroxaban being BSC class-II drug has relatively poor water solubility (about 7 mg/l), causing problems regarding dissolution of Rivaroxaban from the pharmaceutical composition and the oral bioavailability.

There are many approaches available in prior art which can be used to improve dissolution profile of poorly soluble drugs such as hydrophilization, particle size reduction, modification of crystal habit, drug dispersion in carrier, emulsification

etc. There are cases, where such techniques do not improve dissolution to an extent to have any impact on bioavailability and therefore some other techniques or parameters are required for further improvement of dissolution of the drug. A properly designed composition should result in dissolution data that are not highly variable. High variability in results can make it difficult to anticipate in-vivo trends or effects and thus bioavailability of formulation. Dissolution results may be considered highly variable if the relative standard deviation (RSD) is greater than 20% at time points of 10 minutes or less and greater than 10% RSD at later time points. Thus it is equally important to reduce deviation in dissolution test.

US 20080026057 describes a process for the preparation of a solid pharmaceutical composition comprising Rivaroxaban in hydrophilized form, wherein granulate prepared by moist granulation of Rivaroxaban with a hydrophilic binder and a solubilizer is converted to the pharmaceutical composition. Tablets comprising hydrophilized Rivaroxaban are shown to exhibit increased bioavailability as compared with tablets comprising non-hydrophilized Rivaroxaban. However, the moist granulation processes used for hydrophilization of the Rivaroxaban are complex, require special equipment and are difficult to use on an industrial scale. Moreover, they require great amounts of energy for the evaporation of granulation liquid.

US 20100151011 discloses a process for obtaining amorphous and/or meta-stable crystalline modification of Rivaroxaban comprising dissolution and/or melting the Rivaroxaban. In particular, dissolution processes require excessively large amounts of solvent because of the poor solubility of Rivaroxaban in water and pharmaceutically acceptable organic solvents like ethanol or acetone.

Patent application also discloses immediate release forms comprising the use of an amorphous or meta-stable crystalline modification of Rivaroxaban, wherein pharmaceutical composition is prepared by melt extrusion and then dry-granulating the melt-extrudate of Rivaroxaban and other pharmaceutically

acceptable excipients Due to high melting point, process involving melting of Rivaroxaban may result into significant decomposition.

US 20110300214 discloses several methods of dry granulation, pellet layering, Hot melt granulation etc for preparation of composition comprising Rivaroxaban in mixture with a solubilizer and a pseudo-emulsifier.

Further US 20110300214 teaches method of Emulsification of Rivaroxaban by use of solubilizer and emulsifier to increase solubility of poorly soluble Rivaroxaban. Further it teaches hot melt granulation technique in which Rivaroxaban is melted with other excipients at high temperature.
Such process conditions can result into degradation of Rivaroxaban. Moreover, no disclosure of dissolution and bioavailability is mentioned in given patent application.

WO 2010146179 discloses pharmaceutical composition comprising Rivaroxaban prepared by co-milling of Rivaroxaban and one or more pharmaceutically acceptable excipients and dry-mixing with surfactant-filler solid dispersion and compressing into tablet. However, mentioned application is silent about dissolution and bioavailability of said compositions.

CN 103550165 discloses pharmaceutical compositions with improved dissolution rate, which are prepared by granulating pharmaceutically acceptable excipients; and adding micronized rivaroxaban to prepared granules.

In lieu of all these prior knowledge, there is still a need to prepare a stable pharmaceutical composition comprising Rivaroxaban prepared by simple and economically viable process, which provides desired dissolution profile with least deviation.

SUMMARY OF THE INVENTION

One aspect of the present invention is to provide a solid oral dosage form comprising (a) Rivaroxaban and (b) inert granules comprising a hydrophilic polymer, and one or more pharmaceutically acceptable excipient(s), wherein said inert granules are free of Rivaroxaban.

Another aspect of the present invention is to provide a solid oral dosage form comprising (a) co-milled fraction of Rivaroxaban and surfactant (b) inert granules comprising a hydrophilic polymer, and one or more pharmaceutically acceptable excipient(s), wherein said inert granules are free of Rivaroxaban.

Another aspect of the present invention is to provide a solid oral dosage form comprising (a) Rivaroxaban and (b) inert granules comprising a hydrophilic polymer, and one or more pharmaceutically acceptable excipient(s), said solid oral dosage form is obtainable by adding Rivaroxaban and optionally one or more pharmaceutically acceptable excipient(s) with inert granules, wherein said inert granules are free of Rivaroxaban.

Another aspect of the present invention is to provide a solid oral dosage form comprising (a) co-milled fraction of Rivaroxaban and surfactant and (b) inert granules comprising a hydrophilic polymer, and one or more pharmaceutically acceptable excipient(s), said solid oral dosage form is obtainable by adding co-milled fraction of Rivaroxaban and surfactant and optionally one or more pharmaceutically acceptable excipient(s) with inert granules, wherein said inert granules are free of Rivaroxaban.

Yet another aspect of the present invention is to provide a novel process for preparation of a solid oral dosage form comprising Rivaroxaban comprising:

a) Preparing inert granules comprising a hydrophilic polymer and one or more pharmaceutically acceptable excipient(s), by granulation.

b) Adding co-milled fraction of Rivaroxaban and surfactant , optionally with one or more pharmaceutically acceptable excipient(s) with the inert granules prepared in step (a).

c) Optionally adding on or more pharmaceutically acceptable excipient(s) in the mixture/blend of step (b).

d) Preparing a solid oral dosage form from the mixture/blend of step (b) or (c).

wherein, said inert granules are free of Rivaroxaban.

Another aspect of the present invention is to provide a solid oral dosage form comprising rivaroxaban prepared by process comprising

a) Preparation of inert granules comprising a hydrophilic polymer and one or more pharmaceutically acceptable excipient(s), by aqueous granulation.

b) Co-milling Rivaroxaban, a surfactant and optionally one or more pharmaceutically acceptable excipient(s).

c) Adding co-milled fraction of Rivaroxaban prepared in step (b) with said inert granules prepared in step (a).

d) Optionally adding one or more pharmaceutically acceptable excipient(s) with said mixture/blend prepared in step (c).

e) Compressing the resultant mixture/blend of step (c) or (d) into tablets.

FIGURES:

Figure1: Dissolution profiles of composition prepared according to Example-1 (10 mg) and Xarelto® (Batch No. 13AG700)

Figure2: Dissolution profiles of composition prepared according to Example 1 (20 mg) and Xarelto® (Batch No. 13DG916)

DETAILED DESCRIPTION OF INVENTION:

The term "Rivaroxaban" as used herein includes Rivaroxaban free base, its pharmaceutically acceptable salt. Preferably, Rivaroxaban is Rivaroxaban free base. Particle size of Rivaroxaban or its pharmaceutical acceptable salt used

according to present invention is D90, which ranges from 1 micron to 50 microns. Preferably, micronized Rivaroxaban or its pharmaceutical acceptable salt with D90 of less than 10 microns is used. Most preferably, D90 of Rivaroxaban or its pharmaceutical acceptable salt is less than 5 microns. Rivaroxaban can be used in any crystalline, partly crystalline or amorphous form or modification. Preferably, Rivaroxaban is used in the form of crystalline modification I.

The term "D90" as used herein means at least 90% of the particles have volume diameter in the specified range when measured by a suitable method for example laser diffraction using a Malvern Mastersizer™ laser diffraction instrument.

The term "pharmaceutically acceptable excipient(s)" as used herein refers to additive(s) useful for converting pharmacologically active compound into pharmaceutical dosage forms which are suitable for administration to patients. Suitable pharmaceutically acceptable excipients include fillers, binders, surfactants, disintegrants, lubricants, glidants and coloring agents. Other pharmaceutically acceptable excipients can also be included.

The term "inert granules" which is free of Rivaroxaban as used herein means a component wherein Rivaroxaban is not added during processing. Inert granules according to present invention can be prepared by any known process in the art. Preferably, inert granules are prepared by aqueous granulation, wherein Rivaroxaban is not added during granulation.

The term "free of" as used herein refers to Rivaroxaban is not added into inert granules during granulation. The term excludes the Rivaroxaban which is adsorbed or absorbed inside the said inert granules after its preparation.

The term "added" or "mixed" or "adding" or "mixing" as used herein are to be interpreted inclusively, unless the context requires otherwise. That is, the use of these words may imply mixing or adding or granulating Rivaroxaban or one or

more pharmaceutically acceptable excipient(s) with said inert granules or other pharmaceutically acceptable excipient(s) to prepare mixture or blend.

The term "co-milled" as used herein refers to rivaroxaban is milled along with other pharmaceutically acceptable excipient(s), preferably with surfactant. Co-milling of Rivaroxaban and surfactant is preferably performed in dry state. Dry state milling can be achieved by using dry mills such as cutting mills, hammer mills, ball mills, jet mills, particularly Air-Jet mills.

In an embodiment, the solid oral dosage form of Rivaroxaban comprises inert granules comprising a hydrophilic polymer, at least one filler and at least one surfactant. Surprisingly, it was found that a hydrophilic polymer when used in the inert granules can significantly improve dissolution profile of Rivaroxaban, without opting for hydrophilization of Rivaroxaban.

A pharmaceutical composition according to present invention is a solid composition for immediate release for oral administration and it can be in the form of tablet, powder or capsule. Preferably, said composition is in the form of tablet for oral administration.

For a pharmaceutical composition, it is always desirable to have least deviation in the dissolution profile of a composition to get consistent clinical results. To surprise of inventors, use of hydrophilic polymer in the inert granules not just improves the dissolution profile of the composition but also minimizes the deviation associated with it.

The "hydrophilic polymer" may be selected from celluloses, and other water soluble polymers and hydroxylated compounds. The hydrophilic polymer may include, but not limited to cellulose derived materials such as hydroxypropylcellulose, hydroxypropylmethylcellulose, and hydroxyethylcellulose; water soluble polymers and hydroxylated compounds such

as polyvinylpyrrolidone (Povidone), polyvinyl alcohols and glycols, polyethylene glycol and propylene glycol. The preferred hydrophilic polymer is hydroxypropylmethylcellulose (HPMC) which is available in various grades with viscosity ranging of 1 - 1,00,000 cps. Particularly suitable are grades having viscosity ranging from, for example, 1 – 100 cps.

Filler may be selected from cellulose derivatives such as powdered cellulose, microcrystalline cellulose, silicified microcrystalline cellulose; starch, dibasic calcium phosphate, tribasic calcium phosphate, calcium carbonate; saccharides such as lactose, sucrose or dextrose; sugar alcohols such as mannitol, sorbitol or erythritol; and mixtures thereof. The formulation may incorporate one or more of the above fillers, preferably, lactose and microcrystalline cellulose forms the filler. The diluent may be present in an amount ranging from 1% to 90% by weight of the composition.

Surfactant may be selected from anionic, cationic, non-ionic or amphoteric surfactants or those known to the person skilled in the art. The preferred surfactants according to present invention may include, but not limited to Sodium lauryl sulfate, polyoxyehtylene polyoxypropylene glycol (commercially available under trade name of Poloxamers and Pluronics), polyethylene glycol, polyoxyehtylene glycol and ethers, polysorbates (tweens), glycerol, Sorbitan esters (Spans). The preferred surfactant in the present invention is Sodium lauryl sulfate. The surfactant may be present in an amount ranging from 0.5% to 25% by weight of the composition.

Disintegrant may be selected from calcium carboxymethyl cellulose, cross-linked carboxymethyl cellulose sodium, cross-linked polyvinylpyrrolidone, carboxymethylcellulose sodium, sodium starch glycolate, pregelatinized starch; low-substituted hydroxypropylcellulose; and mixtures thereof. The disintegrant may be present in an amount ranging from 1% to 20% by weight of the composition.

Lubricant may be selected from stearic acid or 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. The lubricant may be present in an amount ranging from 0.25% to 5% by weight of the composition.

In a further embodiment, the process preferably comprises single-stage or multi-stage micronization of Rivaroxaban to obtain Rivaroxaban in micronized form with D90 < 50 microns, preferably D90 < 20 microns, preferably D90 < 10 microns and more preferably D90 < 5 microns. Micronization or Rivaroxaban is performed in dry state. Dry state milling can be achieved by using dry mills such as cutting mills, hammer mills, ball mills, jet mills, particularly Air-Jet mills.

In an embodiment, the process for preparation of solid oral dosage form of Rivaroxaban comprises addition of Rivaroxaban with inert granules optionally with one or more pharmaceutically acceptable excipient(s). It is further provided that micronized Rivaroxaban co-milled with surfactant to form co-milled rivaroxaban and surfactant, fraction of which is added with inert granules. Optionally one or more pharmaceutical acceptable excipient is added in the preparation of co-milled fraction of Rivaroxaban and surfactant. It was observed that use of co-milled fraction of rivaroxaban and surfactant, such as sodium lauryl sulfate helps in getting desired release profile.

Thus, in another embodiment of present invention is provided a solid oral dosage form comprising (a) co-milled fraction of Rivaroxaban and surfactant (b) inert granules comprising a hydrophilic polymer, and one or more pharmaceutically acceptable excipient(s), wherein said inert granules are free of Rivaroxaban.

Inert granules according to present invention can be prepared by any process known in the art such as wet or dry granulation. Preferably, inert granules are prepared by wet granulation, more preferably aqueous granulation.

It is advantageous to use aqueous solvent in preparation of inert granules, as non-aqueous solvents may lead to relatively high amount of residual solvents in the final composition and eventually higher degradation products in pharmaceutical composition.

In a further embodiment, is provided a solid oral dosage form comprising rivaroxaban prepared by process comprising:

a) Preparation of inert granules comprising a hydrophilic polymer and one or more pharmaceutically acceptable excipient(s), by aqueous granulation.
b) Co-milling Rivaroxaban, a surfactant and optionally one or more pharmaceutically acceptable excipient(s).
c) Adding co-milled fraction of Rivaroxaban prepared in step (b) with said inert granules prepared in step (a).
d) Optionally adding one or more pharmaceutically acceptable excipient(s) with said mixture/blend prepared in step (c).
e) Compressing the resultant mixture/blend of step (c) or (d) into tablets.

The order of steps in the process of preparation of pharmaceutical compositions according to present invention is for the purpose of representation only and should not limit the scope of the embodiments with respect to performance of steps in the mentioned sequence.

It is preferred that inert granules are dried before mixing it with co-milled fraction of rivaroxaban and surfactant.

In a preferred embodiment is provided a solid oral dosage form comprising rivaroxaban prepared by process comprising:

a) Preparation of inert granules comprising a hydroxypropylmethylcellulose, lactose, microcrystalline cellulose, sodium lauryl sulfate and croscarmellose sodium by aqueous granulation and then drying.
b) Co-milling Rivaroxaban and sodium lauryl sulfate.
c) Adding co-milled fraction of Rivaroxaban prepared in step (b) with said inert granules prepared in step (a), by dry-mixing.
d) Adding microcrystalline cellulose, croscarmellose sodium and magnesium stearate with said mixture/blend prepared in step (c).
e) Compressing the resultant mixture/blend of step (d) into tablets.

In a further embodiment, it is provided that a process for preparation of pharmaceutical composition comprising Rivaroxaban comprising

a) Preparation of inert granules comprising a hydrophilic polymer and one or more pharmaceutically acceptable excipient(s), by aqueous granulation and then drying.
b) Co-milling Rivaroxaban, a surfactant and optionally one or more pharmaceutically acceptable excipient(s).
c) Adding co-milled fraction of Rivaroxaban prepared in step (b) with said inert granules prepared in step (a), by dry-mixing.
d) Optionally adding one or more pharmaceutically acceptable excipient(s) with said mixture/blend prepared in step (c).
e) Compressing the resultant mixture/blend of step (c) or (d) into tablets.

In a further embodiment, it is provided Co-milled fraction of Rivaroxaban and surfactant, optionally with one or more pharmaceutically acceptable excipient(s) is dry-mixed with inert granules in a blender or high-shear mixer and then compressed into tablets. Optionally coating may also be applied over said tablets.

Coating according to present invention may be functional or non-functional coating, preferably coating is non-functional coating.

Another embodiment of present invention provides use of the composition prepared according to present invention for the prophylaxis and/or treatment of various thromboembolic diseases.

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.

Example-1:

Step 1: Inert Granules preparation:

Table-1

Sr. No.	Ingredient	Qty mg/tab
1	MCC 102	32.10
2	Lactose monohydrate DCL 11	19.80
3	Croscarmellose sodium	2.00
4	Water	q.s.
5	Sodium lauryl sulfate	0.50
6	HPMC 6 cps	1.60
Total		**56.00**

Lactose monohydrate, Microcrystalline cellulose and Croscarmellose sodium were sifted through vibratory sifter. These ingredients were transferred to high shear granulator and mixed.

HPMC and sodium lauryl sulfate were dissolved in sufficient quantity of water. This aqueous solution was poured on to excipient mixture in high shear granulator under stirring. This blend was dried in Fluidized bed dryer and sizing was carried out by oscillating granulator.

Step 2: 10.00mg and 20.00mg of Rivaroxaban (Modification 1) and 2.50mg and 5.00mg of sodium lauryl sulfate for 10mg and 20mg respectively, were sifted and mixed together. The mixture was passed through Air-Jet mill. The co-milled material was then collected from the filter bag. The obtained co-milled fraction was then used for preparation of tablets.

Step 3:

Table-2

Formula		10 mg	20 mg
Sr. No.	Ingredients	Qty mg/tab	Qty mg/tab
1	Inert granules (Step 1)	67.90	55.40
2	Co-milled fraction of Rivaroxaban & Sodium lauryl sulfate (Step 2)	12.50	25.00
3	Croscarmellose sodium	2.00	2.00
4	MCC 102	2.00	2.00
5	Magnesium stearate	0.60	0.60
6	Opadry	2.50	2.50
Total (Coated)		**87.50**	**87.50**

Rivaroxaban (Modification-I) and sodium lauryl sulfate co-milled fraction prepared according to step 2, Croscarmellose sodium and Microcrystalline cellulose were dry-mixed with the inert granules prepared according to step 1. Magnesium stearate was added as lubricant. This dry-mix was then compressed into tablets by rotary compression machine.

Tablets thus formed were coated by Opadry coating system in Neocota.

Example-2

Analogous to Example 1, composition was prepared using pharmaceutically acceptable excipients given in following table.

Step 1: Inert Granules preparation:

Table 3

Sr. No.	Ingredient	Qty mg/tab (10 mg)	Qty mg/tab (15 mg)	Qty mg/tab (20 mg)
1	MCC 102	38.30	23.85	54.90
2	Lactose monohydrate DCL 11	26.00	14.63	25.00
3	Croscarmellose sodium	2.00	1.50	2.00
4	Water	q.s.	q.s.	q.s.
5	Sodium lauryl sulfate	0.50	0.37	0.60
6	HPMC 6 cps	1.10	0.83	2.50
Total		**67.90**	**41.18**	**87.50**

Step 2: 20.00mg of Rivaroxaban (Modification 1) and 5.00mg of sodium lauryl sulfate were sifted and mixed together. The mixture was passed through Air-Jet mill. The co-milled material was then collected from the filter bag. The obtained co-milled fraction was then used for preparation of tablets.

Step 3:

Table-4

Formula		10 mg	15 mg	20 mg
Sr. No.	Ingredients	Qty mg/tab	Qty mg/tab	Qty mg/tab
1	Inert granules (Step 1)	67.90	41.18	54.90
2	Co-milled fraction of Rivaroxaban & Sodium lauryl sulfate (Step 2)	12.50	18.75	25.00
3	Croscarmellose sodium	2.00	1.88	2.50
4	MCC 102	2.00	1.50	2.00
5	Magnesium stearate	0.60	0.45	0.60
6	Opadry	2.50	1.88	2.50
Total (Coated)		**87.50**	**65.64**	**87.50**

Dissolution data:

Dissolution of Example 1 was checked in 900 ml of acetate buffer (pH 4.5) + 0.2% SLS, at 75 rpm using paddle (USP)

Strength: 10 mg

Table-5

Sample	% Drug dissolved						
	Time (Min)	5	10	15	20	30	45
Xarelto® (13AG700)	Mean	73	90	94	95	96	97
	%RSD	6.8	2.3	0.9	0.9	0.7	0.8
Ex-1	Mean	67	94	96	98	99	100
	%RSD	9.9	0.4	0.8	0.7	0.7	0.7

Strength: 20 mg

Table-6

Sample	% Drug dissolved						
	Time (Min)	5	10	15	20	30	45
Xarelto® (13DG916)	Mean	56	92	96	98	99	99
Ex-1	Mean	55	89	93	95	98	101

Observation:

Composition prepared according to present invention which comprises hydrophilic polymer, preferably, HPMC, in inert granules, shows dissolution profile similar to Innovator's product, with least deviation.