The present invention relates to a dry ready to use modified release dosage formulation for Metformin dosage forms and its salts and derivatives thereof, a process for preparing extended release tablet using INSTAMODEL (A43D000041 and A43D000042) manufactured by Ideal Cures Private Limited Mumbai India thereof also use thereof as additive to animal feeds, foods and food supplements and also cosmetic and pharmaceutical compositions. Invention also relates to ready-to-use modified release compositions capable of regulating release of Metformin at various dosage strength, a process for production thereof and also use thereof as formulated pharmaceutical compositions.
Description
EXTENDED RELEASE FORMULATION OF METFORMIN

Technical Field
[1] The present invention relates to a dry ready to use modified release dosage formulation for Metformin dosage forms and its salts and derivatives thereof, a process for preparing extended release tablet using JN STAMODEL (A43 D00041 and A43D00042) manufactured by Ideal Cures Private Limited Mumbai India thereof also use thereof as additive to animal feeds, foods and food supplements and also cosmetic and pharmaceutical compositions. Invention also relates to ready-to-use modified release compositions capable of regulating release of Metformin at various dosage strength, a process for production thereof and also use thereof as formulated pharmaceutical compositions.

Background Art
[2] In general Metformin has been widely prescribed for lowering blood glucose in patients with diabetes. However, being a short acting drug, metformin requires n vo or three times-a-day dosing. Adverse events associated with metformin use are often gastrointestinal, e.g. anorexia, nausea, vomiting and occasionally diarrhea, etc. These adverse effects may be partially avoided by reducing the initial and/or maintenance dose or using an extended-release dosage form.

Metformin has intrinsically poor permeability in the lower portion of the gastrointestinal tract, leading to absorption from the upper part of the tract. It has very high solubility in water (>300 mg/ml at 25°C). These parameters can lead to difficulty in providing a sustained release of the drug from a formulation and the concomitant problems associated with controlling the initial burst from such a formulation. The rate of dissolution of such high solubility drugs may be reduced by embedding the drug in a polymeric matrix or surrounding it with a polymeric barrier membrane through which the drug must diffuse to be released for absorption.

Metformin is administered through solid dosage ranges from 100 mg to 75 mg daily. In standard doses of 100 mg is taken i n daily. Prescription of Metformin recommend that it should be taken with meals if possible and daily. Dosage generally should not exceed 100 mg daily.

In state of the art modified release compositions are developed to provide relatively constant drug plasma levels and sustained efficacy for longer period of time. In principle aim of extended and modified release composition is to get required therapeutic concentration of the active in the blood stream and maintain its therapeutic concentration without deviation from strength during specified period.

In state of art various grades of cellulosic polymers are used in the modified release compositions e.g. HPMC polymer. WO 2014060256, WO 2003039527 and WO 2005123134 disclose the use of hydrophilic polymers like hypromellose for extended
release of drug like metformin. These polymers extend the release of drug by showing osmosis nature in aqueous conditions. Cellulosic matrix based system work by the swelling and gelling function i.e. these polymer swell through influx of liquids and a gel like physical structure is formed which provides extended release effect facilitated by diffusion of the Metformin. Some patents that disclose matrix based systems for slow release of metformin include WO 2007 136 151 and US 5955 106.

In theory it is known that with high viscosity grade polymer after attaining gelling effect drug release is lower but as time progresses drug release is increased. On the contrary with low viscosity grade polymer after attaining gelling effect drug is released at faster speed due to larger pore sized and concentration of drug decrease as time progresses.

In order to minimize difficulties associated in ratios of polymers, batch to batch variations, formulating, storing and preserving many loose components of differently textured and sized ingredients have been in industry to make ready to use extended release or modified release composition which are convenient to handle.

The object of the present invention is to provide a ready-to-use matrix system and method of preparation for Metformin extended release or modified release formulation.

Disclosure of Invention

Summary of Invention

Accordingly, the present invention provides hydrophilic matrix system based ready to use technology for Modified or Extended Release Formulation of Metformin Hydrochloride using INSTAMODEL (A43 D00041 and A43 D00042) manufactured by Ideal Cures Private Limited Mumbai India.

Accordingly, the present invention also provides method for making ready to use Metformin modified or extended release formulation, involving steps of aqueous granulation, drying, lubrication and punching of tablets.

In another aspect, present invention also provides Twice a day Metformin table dosage form.

Extended release or modified release tablet formulation can be in the form of single or multilayer tablets, capsule shaped oral dosage form, caple, granules, disc, pellets, granules in capsule, mini-tablets in oral dosage form and other possible oral dosage form mean thereof.

In yet another embodiment, the solid oral dosage form can optionally include one or more pharmaceutically acceptable excipients.

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

Detailed Description

Below description specify various scientific terms unless stated with context, all
technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art, to which this invention belongs. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, the preferred methods and materials are described.

[17] Unless stated to the contrary. The feature 'ready-to-use', in the context of the present invention, is taken to mean the property that the composition according to the invention can be used directly for its purposes by the user by simply dispersing it in required quantity of water.

[18] The term 'modified release' is in context of the invention as a way of active drug delivery where the rate of release of the active drug from the composition is not exclusively dependent on the concentration of active drug remaining in the dosage form and/or the solubility of the active drug in the liquid surrounding the composition, and where the time course with or without respective location of release of active drug from an oral dosage form are chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms. For the purpose of invention active drug is selected from Aceclofenac, its intermediates and derivatives thereof.

[19] The term 'Aceclofenac' is in context of the invention includes its polymorphic forms, the pharmaceutically acceptable salts, including salts esters and other chemical derivatives or intermediates etc. The solid pharmaceutical composition comprises Aceclofenac from 1 to 80 w/w % of dosage form.

[20] The term 'dosage' 'solid pharmaceutical composition' may include one or more of tablet, capsule, powder, disc, caplet, granules, pellets, granules in capsule, minitablets, minitablets in capsule, pellets in capsule, sachet and the like. The solid pharmaceutical composition also includes multilayer tablets. The solid pharmaceutical compositions are meant for oral administration.

[21] The term 'tablet' includes pharmaceutical compositions of all shapes and sizes, whether coated or uncoated.

[22] The term 'Lubricant' in the context of the present invention, is taken to mean that an ingredient added to prevent the adhesion of tablet materials to the punches and dies, reduce inter-particle friction and facilitate the ejection of oral dosage forms from the die cavity. Lubricant of present invention includes but not limited to talc, magnesium stearate, stearic acid, sodium stearyl fumarate and there derivatives thereof.

[23] The term 'Glidant' in the context of the present invention, is taken to mean that an ingredient which enhance product flow by reducing inter-particulate friction. Glidant can be used in present invention includes but not limited to silicon di-oxide, colloidal silicon dioxide and there derivatives thereof. It is available under several brand names like AEROSIL® and CAB-O-SIL®.

[24] The term 'Solvent' in the context of the present invention, is taken to mean an ingredient that facilitate mixing of components in wet granulation process. Solvent can
be used in present invention includes but not limited to Acetone, ethanol, methylene di chloride, isopropyl alcohol, water or their mixture thereof.

[25] The term 'Binder' or 'Binding agent' in the context of the present invention, is taken to mean ingredient that facilitate binding of components in wet granulation process. Solvent can be used in present invention includes but not limited to dextrin and their derivatives, inaltodextrin, polyvinyl polymers, Polyvinyl pyrrol idone K30 (PVP K.30) and there derivatives thereof.

[26] The ready to use polymeric composition Instamodel A43D00045 for extended and modified release formulation was supplied by Ideal Cures Private Limited, Mumbai, www.idealcures.co.in. This product was used to create inventive dosage form having ideal modified release profile for twice a day administration.

[27] According to inventors it was surprisingly found that extended release solid oral dosage form for Aceclofenac can be created with ready to use Instamodel (A43D00045) system and dosage form have advantageous modified release properties. The ready to use composition in accordance with present invention comprise INSTAMODEL (A43D00045). In one of the embodiment of present invention Aceclofenac is formulated with ready to use composition to prepare modified release dosage form. In accordance with present invention different solvents, derivatives, polymorphs of Aceclofenac could be combined to achieve ready-to-use composition to achieve extended or modified release dosage form.

[28] In a dosage form according to the invention Aceclofenac is blended with the ready to use polymer and aqueous granulated further the granulated mixture is compressed to produce a solid formulation. The ingredients are blended to form a uniform powder and then compressed with means generally known to skilled in the art.

[29] In yet another embodiment of present invention Aceclofenac and INSTAMODEL are blended together with binding agent and thereafter wet granulated and dried. These dried granules are then processed in presence of lubricant and glidant, and thereafter compressed to form appropriate dosage form and finally coated.

[30] In yet another embodiment of present invention Aceclofenac and INSTAMODEL are blended together with binding agent and thereafter wet granulated and dried. These dried granules are then processed in presence of lubricant and glidant, and thereafter compressed to form appropriate dosage form and optionally coated.

[31] This system of formulation uses simple and economic polymers hence cost effective to the customer. Another advantage of the present formulation is its robust and reproducible results for extended release dose form without batch to batch variations. Further by using aqueous solvent system for granulation dosage form does not have any residual solvent or hazardous effect found in many organic solvent based formulations.

[32] Inventive dosage form may be prepared by blending Aceclofenac, their derivatives or combination thereof along with ready to use composition. Therefore inventive for-
mulation preparation comprise steps as:-

Below description specify various scientific terms unless stated with context, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art, to which this invention belongs. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, the preferred methods and materials are described.

Unless stated to the contrary, The feature 'ready-to-use', in the context of the present invention, is taken to mean the property that the composition according to the invention can be used directly for its purposes by the user by simply dispersing it in required quantity of water.

The term 'modified release' is in context of the invention as a way of active drug delivery where the rate of release of the active drug from the composition is not exclusively dependent on the concentration of active drug remaining in the dosage form and / or the solubility of the active drug in the liquid surrounding the composition, and where the time course with or without respective location of release of active drug from an oral dosage form are chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms. For the purpose of invention active drug is selected from Metformin, its intermediates and derivatives thereof.

The term 'Metformin' is in context of the invention includes its polymorphic forms, the pharmaceutically acceptable salts, including salts esters and other chemical derivatives or intermediates etc. The solid pharmaceutical composition comprises Metformin from 1 to 90 w/w % of dosage form.

The term 'dosage', 'solid pharmaceutical composition' may include one or more of tablet, capsule, powder, disc, caplet, granules, pellets, granules in capsule, minitablets, minitablets in capsule, pellets in capsule, sachet and the like. The solid pharmaceutical composition also includes multilayer tablets. The solid pharmaceutical compositions are meant for oral administration.

The term 'tablet' includes pharmaceutical compositions of all shapes and sizes, whether coated or uncoated.

The term 'Lubricant' in the context of the present invention, is taken to mean that an ingredient added to prevent the adhesion of tablet materials to the punches and dies, reduce inter-particle friction and facilitate the ejection of oral dosage forms from the die cavity. Lubricant of present invention includes but not limited to talc, magnesium stearate, stearic acid, sodium stearyl fumarate and there derivatives thereof.

The term 'Glidant' in the context of the present invention, is taken to mean that an ingredient which enhance product flow by reducing inter-particle friction. Glidant can be used in present invention includes but not limited to silicon di-oxide, colloidal silicon dioxide and there derivatives thereof. It is available under several brand names like AEROSIL® and CAB-O-SIL®.
The term 'Solvent' in the context of the present invention, is taken to mean ingredient that facilitate mixing of components in wet granulation process. Solvent can be used in present invention includes but not limited to Acetone, ethanol, methylene dichloride, isopropyl alcohol, water or their mixture thereof.

The term 'Binder' or 'Binding agent' in the context of the present invention, is taken to mean ingredient that facilitate binding of components in wet granulation process. Solvent can be used in present invention includes but not limited to dextrin and their derivatives, maltodextrin, polyvinyl polymers, Polyvinyl pyrrol idone K30 (PVP K30) and there derivatives thereof.

The ready to use polymeric composition Instamodel A43D0004 1 and A43 D00042 for extended and modified release formulation was supplied by Ideal Cures Private Limited, Mumbai, www.idealcures.co.in. This product was used to create inventive dosage form having ideal modified release profile for Once a day administration.

According to inventors it was surprisingly found that extended release solid oral dosage form for Metformin can be created with ready to use Instamodel (A43D00041 and A43D00042) system and dosage form have advantageous modified release properties, The ready to use composition in accordance with present invention comprise INSTAMODEL (A43D0004 1 and A43 D00042). Instamodel blends combination can be used in plurality of layers and combinations including but not limited to various combinations and orders of mixings or granulations. In one of the embodiment of present invention Metformin is formulated with ready to use composition to prepare modified release dosage form. In yet another embodiment metformin is formulated with ready to use composition with different grades and orders of mixing and granulations. In accordance with present invention different salts, derivatives, polymorphs of Metformin could be combined to achieve ready-to-use composition to achieve extended or modified release dosage form.

In a dosage form according to the invention Metformin is blended with the ready to use polymer and aqueous granulated further the granulated mixture is compressed to produce a solid formulation. The ingredients are blended to form a uniform powder and then compressed with means generally known to skilled in the art.

In yet another embodiment of present invention Metformin and INSTAMODEL are blended together with binding agent and thereafter wet granulated and dried. These dried granules are then processed in presence of lubricant and glidant, and thereafter compressed to form appropriate dosage form and finally coated.

In yet another embodiment of present invention Metformin and INSTAMODEL are blended together with binding agent and thereafter wet granulated and dried. These dried granules are then processed in presence of lubricant and glidant, and thereafter compressed to form appropriate dosage form and optionally coated.

This system of formulation uses simple and economic polymers hence cost effective to the customer. Another advantage of the present formulation is its robust
and reproducible results for extended release dose form without batch to batch variations. Further by using aqueous solvent system for granulation dosage form does not have any residual solvent or hazardous effect found in many organic solvent based formulations.

Inventive dosage form may be prepared by blending Metformin, their derivatives or combination thereof along with ready to use composition. Therefore inventive 6 formulation preparation comprise steps as:-

1. Blending of ready to use formulation Instamold (A43 D0004 1) with Metformin.
2. Thorough mixing to form dry powder
3. Wet granulation with active drug and solvent
4. Sieving through appropriate size
5. Tray drying or fluidized bed drying
6. Again blending with ready to use formulation instamold (A43 D00042)
7. Optionally addition of lubricant
8. Final tablet compression
9. Optional film coating

According to one of the embodiment inventive dosage form is prepared by blending ready to use composition (Instamodel A43D0004 1 and A43 D00042), process blending is performed by conventional dry blender or a food processor or 'V-blender' or a similar function device. Further Metformin are processed using aqueous solvent with binder through wet granulation or a similar wet mixing method to generate dosage formulation. Dosage formulation is further dried, sieved and compressed optionally with addition of lubricant, binder, glidant to form modified release oral dosage form.

In one of the embodiment of present invention, inventive dosage formulations are prepared by blending Metformin along with Instamodel (A43D0004 1 and A43D00042). Initially all components are blended by conventional dry blending in a food processor or 'V-blender' or a similar function device. Other solid oral dosage formulation components like binders, lubricants, glidants, detackifier, excipients can be added to create inventive formulation. Further mixture is then processed with appropriate quantity of aqueous solvent with binder and wet granulated. Obtained sieved granulated is then uniformly mixed with premeasured amount of the lubricant to improve industrial acceptability and oral dosage compression quality. Subsequently uniform mixed inventive formulation is compressed in standard pharmacopeial equipment to get a controlled release oral dosage formulation of the correct desired weight and strength.

In yet another embodiment Metformin is formulated comprising steps of mixing Instamold with Metformin with solvents, granulating and drying to granulation which
is subsequently sifted using appropriate mesh screen. Further generated granules can be again blended with instamol to generate plurality of layers. Finally generated granules are sifted and blended with lubricants.

According to one of the main embodiment wherein hardness of tablets produced is in range of 5 Kg/cm\(^2\) to 30 Kg/cm\(^2\). In one of the embodiment oral dosage forms produced by inventive composition having human administrable active ingredient is suitable for human use. Alternatively drug suitable for veterinary purpose formulated in accordance with present composition will be suitable for veterinary use.

According to the objective of present invention Metformin is formulated in oral dosage form for modified or extended release delivery. Inventions composition comprising 250, 500, 750, 800, 1000 mg or 1500 mg of Metformin in plurality of dosage formulations. Controlled release formulation can have combination of one or more additional drugs.

Suitable APIs that can be used with the present invention include, but are not limited to: adrenergic blocking agent; acetyl-cholinesterase inhibitor; analgesic or antipyretics; angiotensin modulator; anthelmintic agents; ant anxiety agent; antibacterial; antibiotic; anticoagulant; anticonvulsant; antidepressant; anti fungal; anti-histamine; antimalarial; antimicrobial agent; antipsychotic agent; Antiviral agents; blood glucose lowering drug; calcium channel modulator; diuretic; erectile dysfunction; gastric acid secretion inhibitor; histamine H2-receptor antagonist; inhibitor of steroid Type II 5[alpha]-reductase including; lipid regulating agents; selective H1-receptor antagonist; vasodilator; vitamins.

Following examples are offered to more fully illustrate the invention, but are not to be construed as limiting the scope thereof.

**Mode for invention**

**Example 1.**

**Preparation of Metformin Hydrochloride modified release tablets (500 mg)**

The dosage formulation for 100,000 (86.00 kg) Tablets of Metformin is prepared using composition as stated in table:- 1 wherein Metformin is 50.0 kg and 1.20 kg of Instamol (A43D0004 1) are weighed, sifted in rapid mixture granulator accordingly, subsequently sieved to get uniformly granulated powder through 40 mesh screen. It is noted that other size screen could be used to get similar results. Sieved Metformin with above ingredients is granulated using water as granulating solvent in rapid mixture granulator (RMG). It is recommended that RMG should be at slow speed for 15 min followed by high speed for 3-5 mins. Granulation step requires proper optimization of water quantity and continuous monitoring to avoid heavy granulation. If required extra water can be added gradually under continuous observation (to avoid heavy wet mass). Generated wet mass is sieved using #20 screen (Multi-mill/ Fitzmi II) dried in tray drier (or Fluidized. bed dryer) at temperature not more than 50\(^\circ\)C-55\(^\circ\)C keeping loss on drying at 1-2%. Subsequently sift the dried granule using #30 mesh sieve on vibratory
sifter and again sift on 1.0 mm screen at slow speed.

Further Mix the dried granule with 23.90 kg of Instamodl blend II (A43 D00042) for 10 min in a suitable blender (octagonal blender).

Table 1

<table>
<thead>
<tr>
<th>Formulation ingredients</th>
<th>Composition</th>
<th>Quantity for Batch size of 100,000 Tabs.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% w/w</td>
<td>mg/tablet</td>
</tr>
<tr>
<td>Metformin HCl</td>
<td>58.14 %</td>
<td>5000</td>
</tr>
<tr>
<td>Instamodl -l (A43D00041)</td>
<td>13.02 %</td>
<td>1120</td>
</tr>
<tr>
<td>Purified water</td>
<td>q.s</td>
<td>q.s</td>
</tr>
<tr>
<td>Instamodl-II (A43D00042)</td>
<td>27.79 %</td>
<td>2390</td>
</tr>
<tr>
<td>Magnesium Stearate,</td>
<td>0.58 %</td>
<td>3.0</td>
</tr>
<tr>
<td>Colloidal silicon dioxide</td>
<td>0.47 %</td>
<td>4.0</td>
</tr>
<tr>
<td>Total</td>
<td>100.00</td>
<td>860.0</td>
</tr>
</tbody>
</table>

Coating ingredients

<table>
<thead>
<tr>
<th>Item</th>
<th>Quantity</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Instacoat Universal (ICU-3849) white</td>
<td>20β</td>
<td>2.580 kg(include 20 % extra &gt;compensate process losses)</td>
</tr>
<tr>
<td>Purified water</td>
<td>20.87 kg</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>880.70</td>
<td></td>
</tr>
</tbody>
</table>

To promote efficient tablet punching further 0.50 kg of magnesium stearate and 0.40 kg of colloidal silicon dioxide sieved through 40 mesh screen is added to above dried blended formulation in blender for subsequent 5 minutes. Final screened granules are compressed using 18.0 mm x 9.0 mm, capsule shaped, standard concave punches (for 860 mg average weight) circular, standard concave circular punches using Karnavati Tablet Compression M/C-17 Stn. GM.P machine at hardness not less than 15-25 kg/cm². 7. The tablets are subjected to film coating using suitable film coating system. Film coating is done with normal immediate release film coating system i.e. Instacoat Universal (1CU-3849 White) for weight gain of 2.0 - 2.5 % w/w. Generated dosage form tablets are then subjected to film coating using Instacoat Universal. Coating composition is weighed in accordance with table 1 and 11% coating suspension prepared in water with stirrer and mixed for about 45 minutes subsequently it is passed through 80 mesh screen. Coating is preformed on dosage form using INSTACOAT Pharma R&D coater (6 pan) at 25 rpm with inlet temperature being 53 °C and bed temperature at 40 °C. coating was done using 1mm nozzle sprayer with peristaltic pump injecting coating suspension at the rate of 1ml/min. Coated tablets are then dried and packed as per pharmacopoieal guidelines.

Example 2
Dissolution Profile Evaluation of Metformin tablet

Metformin dose form dissolution study was performed. Drug dissolution profiles of tablet prepared are measured by USP 35 dissolution test of rotating basket method <711>. It is evident from standard state of the art that active ingredient may have its own dissolution testing parameters which can be found in their respective monographs. The active ingredient content for present invention is standardized for sustained release profile is as per table 2:-

Medium: Phosphate buffer pH 6.8; 1000 ml

Time interval: 1, 2, 3, 6 and 10 hour (Test 1 & Test 2 of USP/NF 35, 2012.)

Table 2

<table>
<thead>
<tr>
<th>Time (Hour)</th>
<th>Acceptance Limits USP</th>
<th>Acceptance Limits IP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20% - 40%</td>
<td>25% - 50%</td>
</tr>
<tr>
<td>2</td>
<td>35% - 55%</td>
<td>..NA..</td>
</tr>
<tr>
<td>3</td>
<td>45% - 65%</td>
<td>45 - 75 %</td>
</tr>
<tr>
<td>6</td>
<td>65% - 85%</td>
<td>..NA..</td>
</tr>
<tr>
<td>10</td>
<td>NLT 85%</td>
<td>NLT 80%</td>
</tr>
</tbody>
</table>

The mean values are shown Sample size is of 10 tablets

It was observed that it shows maximum absorbance at 284 nm on Double Beam UV-VIS Spectrophotometer (UV 2700- Thermo Fisher Scientific).

METFORMIN IN VITRO % DRUG RELEASE USING INSTAMODEL
(A43D00041 AND A43D00042) DISSOLUTION COMPARISON

<table>
<thead>
<tr>
<th>Time Intervals (inclusive of Test 1 &amp; test 2 of USP) in hours</th>
<th>Dissolution Limits</th>
<th>Ref Product: CetapinXR 500 mg (% Drug released)</th>
<th>Product: Metformin 500 mg using Instamode blend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Min</td>
<td>Max</td>
</tr>
<tr>
<td>1</td>
<td>20% - 40%</td>
<td>26.65</td>
<td>28.31</td>
</tr>
<tr>
<td>2</td>
<td>35% - 55%</td>
<td>42.64</td>
<td>44.65</td>
</tr>
<tr>
<td>3</td>
<td>45% - 65%</td>
<td>54.72</td>
<td>56.26</td>
</tr>
<tr>
<td>6</td>
<td>65% - 85%</td>
<td>70.17</td>
<td>79.24</td>
</tr>
<tr>
<td>10</td>
<td>NLT 85%</td>
<td>95.94</td>
<td>102.22</td>
</tr>
</tbody>
</table>
The drug dissolved profile of the Reference products and Metformin having dose strength of 500 mg using instamod (A43D00041 and A43D00042) formulations are compared. The release exponents for the Reference and formulated Metformin is found to be having similar modified release profile indicating a predominantly diffusion based drug release mechanism.
Claims


[2] The solid pharmaceutical composition of claim 1, wherein Metformin can be in form of salt, polymorphic form, its derivatives or mixture thereof.

[3] The solid pharmaceutical composition of claim 1, wherein binder is selected from polyvinyl polymers, Polyvinyl pyrrolidone K30 (PVP K30) and like.

[4] The solid pharmaceutical composition of claim 1, wherein solvent is selected from water, isopropyl alcohol and like.

[5] The solid pharmaceutical composition of claim 1, wherein lubricant is selected from talc, magnesium stearate, stearic acid, sodium stearyl fumarate and combination thereof.

[6] The solid pharmaceutical composition of claim 1, wherein glidant is selected from silicon di-oxide, colloidal silicon dioxide and there derivatives thereof.

[7] A process for preparing Metformin tablet according to claim 1 comprising
   a. Blending Instamodol (A43D0004 1) with Metformin
   b. Thorough mixing and Wet granulation with binder and solvent
   c. Sieving and drying
   d. Again Blending with Instamodol (A43D00042)
   e. Addition of lubricant and glidant
   f. Final tablet compression
   g. Optional film coating.

[8] The solid pharmaceutical composition prepare using process for preparing Metformin tablet according to claim 1 comprising
   a. Blending Instamodol (A43D0004 1) with Metformin
   b. Thorough mixing and Wet granulation with binder and solvent
   c. Sieving and drying
   d. Again Blending with Instamodol (A43D00042)
   e. Addition of lubricant and glidant
   f. Final tablet compression
   g. Optional film coating.
INTERNATIONAL SEARCH REPORT

International application No.
PCT/IN2014/000602

A. CLASSIFICATION OF SUBJECT MATTER
   A61K3 1/155, A61K9/16, A61K9/2 0 Version=2014 .01

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
   A 6 1 K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
   IPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
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<td>WO2006082523 A2 (AUROBINDO PHARMA LTD [IN]) 10 AUGUST 2006 (10-08-2006) The whole document</td>
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<td>Y</td>
<td>IDEAL CURE PVT LTD:&quot;Extended Release Tablets Formulation Simplified&quot; 19 JULY 2012 (19/07/2012)</td>
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Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents:
  "A" document defining the general state of the art which is not considered to be of particular relevance
  "E" earlier application or patent but published on or after the international filing date
  "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
  "O" document referring to an oral disclosure, use, exhibition or other means
  "P" document published prior to the international filing date but later than the priority date claimed
  "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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  "&" document member of the same patent family

Date of the actual completion of the international search
02-03-2015

Date of mailing of the international search report
02-03-2015

Name and mailing address of the ISA/Indian Patent Office
Plot No. 31, Sector 14, Dwarka, New Delhi-110075

Authorized officer
K Janardana

Facsimile No.
Telephone No. +91-1125300200

Form PC17ISA/210 (second sheet) (January 2015)
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