Office of the Controller General of Patents, Designs & Trade Marks
Department of Industrial Policy & Promotion,
Ministry of Commerce & Industry,
Government of India

# (http://ipindia.nic.in/index.htm)

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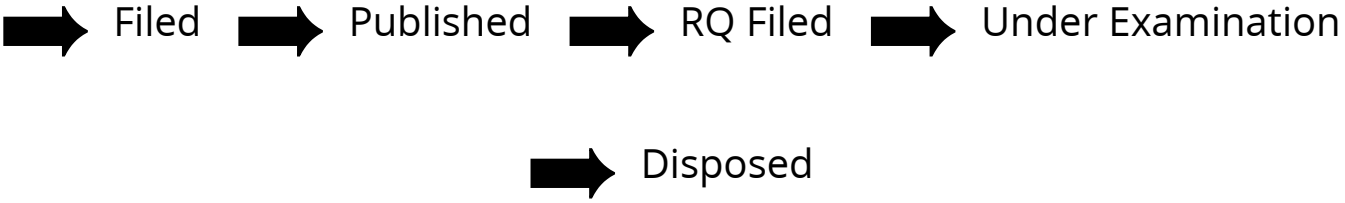
| Application Details | |
|---|---|
| APPLICATION NUMBER | 202121035760 |
| APPLICATION TYPE | ORDINARY APPLICATION |
| DATE OF FILING | 07/08/2021 |
| APPLICANT NAME | 1 . DR. SHUBHRAJIT MANTRY<br>2 . MISS. PALLAVI BHIMAJI GHOLAP<br>3 . DR. SUMIT ASHOK JOSHI<br>4 . DR. GANESH YOGIRAJ DAMA<br>5 . DR. SHRIRAM RAMESH PETHAKAR |
| TITLE OF INVENTION | IMMEDIATE RELEASE TABLET OF ENALAPRIL MALEATE |
| FIELD OF INVENTION | CHEMICAL |
| E-MAIL (As Per Record) | vijay@patlex.in |
| ADDITIONAL-EMAIL (As Per Record) | vijay@patlex.in |
| E-MAIL (UPDATED Online) | |
| PRIORITY DATE | |
| REQUEST FOR EXAMINATION DATE | -- |
| PUBLICATION DATE (U/S 11A) | 10/09/2021 |

| Application Status | |
|---|---|
| APPLICATION STATUS | Awaiting Request for Examination |

| | | | |
|---|---|---|---|
| | | | View Documents |




In case of any discrepancy in status, kindly contact ipo-helpdesk@nic.in

# पेटेंट कार्यालय
# शासकीय जर्नल

# OFFICIAL JOURNAL
# OF
# THE PATENT OFFICE


| | | |
|---|---|---|
| निर्गमन सं. 37/2021 | शुक्रवार | दिनांक: 10/09/2021 |
| ISSUE NO. 37/2021 | FRIDAY | DATE: 10/09/2021 |



पेटेंट कार्यालय का एक प्रकाशन
PUBLICATION OF THE PATENT OFFICE

(12) PATENT APPLICATION PUBLICATION
(19) INDIA
(22) Date of filing of Application :07/08/2021

(21) Application No.202121035760 A
(43) Publication Date : 10/09/2021

(54) Title of the invention : IMMEDIATE RELEASE TABLET OF ENALAPRIL MALEATE

| | |
|---|---|
| (51) International classification | :A61K0009200000, A61K0031401000, A61K0047260000, A61K0038550000, A61K0009460000 |
| (31) Priority Document No | :NA |
| (32) Priority Date | :NA |
| (33) Name of priority country | :NA |
| (86) International Application No<br>Filing Date | :NA<br>:NA |
| (87) International Publication No | : NA |
| (61) Patent of Addition to Application Number<br>Filing Date | :NA<br>:NA |
| (62) Divisional to Application Number<br>Filing Date | :NA<br>:NA |

(71)**Name of Applicant :**
**1)DR. SHUBHRAJIT MANTRY**
Address of Applicant :Shri Gajanan Maharaj Shikshan Prasarak Mandal™s Sharadchandra Pawar College of Pharmacy At: Dumbarwadi, Post : Khamundi, Tal: Junnar, Pune Maharashtra India
**2)MISS. PALLAVI BHIMAJI GHOLAP**
**3)DR. SUMIT ASHOK JOSHI**
**4)DR. GANESH YOGIRAJ DAMA**
**5)DR. SHRIRAM RAMESH PETHAKAR**
(72)**Name of Inventor :**
**1)DR. SHUBHRAJIT MANTRY**
**2)MISS. PALLAVI BHIMAJI GHOLAP**
**3)DR. SUMIT ASHOK JOSHI**
**4)DR. GANESH YOGIRAJ DAMA**
**5)DR. SHRIRAM RAMESH PETHAKAR**

(57) Abstract :
IMMEDIATE RELEASE TABLET OF ENALAPRIL MALEATE The present invention is related to an immediate release tablet of Enalapril Maleate and the process of preparing the tablet by direct compression method. The present invention provides an immediate release tablet of Enalapril Maleate providing disintegration time of 13 seconds and drug release of 98% in 20 minutes for lowering blood pressure and to treat symptomatic and asymptomatic left ventricular dysfunction.

No. of Pages : 24 No. of Claims : 7


महाराष्ट्र MAHARASHTRA ◐ 2020 ◐ BC 695644

LATUR TREASURY 01 JUL 2021 Stamp H.C./Sr.Clerk

कार्यालय

# FORM FOR AUTHORISATION OF A PATENT AGENT/OR ANY PERSON IN A MATTER OR PROCEEDING UNDER THE ACT

Power of Attorney by **DR. SHUBHRAJIT MANTRY, MISS. PALLAVI BHIMAJI GHOLAP, DR. SUMIT ASHOK JOSHI, DR. GANESH YOGIRAJ DAMA** and **DR. SHRIRAM RAMESH PETHAKAR** in the name of **Vijaykumar Shivpuje** of the address **Sri Kripa, Akshay Nagar, Old Ausa Road, Latur, 413531, Maharashtra, India** in respect of the patent application filing and prosecution in India.

**FORM 26**

THE PATENTS ACT, 1970

(39 of 1970)

&

THE PATENT RULES, 2003

**FORM FOR AUTHORISATION OF A PATENT AGENT/OR**

**ANY PERSON IN A MATTER OR PROCEEDING UNDER THE ACT**

(See sections 127 and 132; rule 135)

We

| Name | Nationality | Address |
|---|---|---|
| DR. SHUBHRAJIT MANTRY | Indian | Shri Gajanan Maharaj Shikshan Prasarak Mandal's Sharadchandra Pawar College of Pharmacy, At: Dumbarwadi, Post: Khamundi, Tal: Junnar, Dist: Pune – 410504, Maharashtra, India. |
| MISS. PALLAVI BHIMAJI GHOLAP | Indian | Shri Gajanan Maharaj Shikshan Prasarak Mandal's Sharadchandra Pawar College of Pharmacy, At: Dumbarwadi, Post: Khamundi, Tal: Junnar, Dist: Pune – 410504, Maharashtra, India. |
| DR. SUMIT ASHOK JOSHI | Indian | Shri Gajanan Maharaj Shikshan Prasarak Mandal's Sharadchandra Pawar College of Pharmacy, At: Dumbarwadi, Post: Khamundi, Tal: Junnar, Dist: Pune – 410504, Maharashtra, India. |
| DR. GANESH YOGIRAJ DAMA | Indian | Shri Gajanan Maharaj Shikshan Prasarak Mandal's Sharadchandra Pawar College of Pharmacy, At: Dumbarwadi, Post: Khamundi, Tal: Junnar, Dist: Pune – 410504, Maharashtra, India. |
| DR. SHRIRAM RAMESH PETHAKAR | Indian | Shramjivi Shikshan Prasarak Mandal's Shramjivi College of Pharmacy, Omerga, Dist: Osmanabad – 413606, Maharashtra, India. |

hereby authorize **Vijaykumar Shivpuje (IN-PA 1096)** of the address **Sri Kripa, Akshay Nagar, Old Ausa Road, Latur, 413531, Maharashtra, India** to act our behalf, as our agent, in connection with Granted patents and pending applications or any future cases, their renewals and maintenance, objections, oppositions, rectifications, cancellations, assignments and other matters and proceedings relating thereto and to receive all notices, requisitions and communications until further notice.

We further authorize our said agents to appoint any person or persons on our behalf to do all what is necessary in the matters and proceedings. We hereby revoke all previous authorizations, if any made, in respect of, same matter or proceeding.

Dated this 06th August 2021

| Name | Signature |
|---|---|
| **DR. SHUBHRAJIT MANTRY** |  |
| **MISS. PALLAVI BHIMAJI GHOLAP** |  |
| **DR. SUMIT ASHOK JOSHI** |  |
| **DR. GANESH YOGIRAJ DAMA** |  |
| **DR. SHRIRAM RAMESH PETHAKAR** |  |

To,

The Controller of Patent,

The Patent Office, at...**Mumbai**...

| | |
|---|---|
| **FORM 3**<br>**THE PATENTS ACT, 1970**<br>**(39 OF 1970)**<br>**and**<br>**THE PATENTS RULES, 2003**<br>**STATEMENT AND UNDERTAKING UNDER SECTION 8**<br>**[See section 8, rule 12]** | |
| 1. Name of the applicant (s), | ~~I~~/We<br>**DR. SHUBHRAJIT MANTRY**<br>Shri Gajanan Maharaj Shikshan Prasarak Mandal's Sharadchandra Pawar College of Pharmacy, At: Dumbarwadi, Post: Khamundi, Tal: Junnar, Dist: Pune – 410504, Maharashtra, India.<br>**MISS. PALLAVI BHIMAJI GHOLAP**<br>Shri Gajanan Maharaj Shikshan Prasarak Mandal's Sharadchandra Pawar College of Pharmacy, At: Dumbarwadi, Post: Khamundi, Tal: Junnar, Dist: Pune – 410504, Maharashtra, India.<br>**DR. SUMIT ASHOK JOSHI**<br>Shri Gajanan Maharaj Shikshan Prasarak Mandal's Sharadchandra Pawar College of Pharmacy, At: Dumbarwadi, Post: Khamundi, Tal: Junnar, Dist: Pune – 410504, Maharashtra, India.<br>**DR. GANESH YOGIRAJ DAMA**<br>Shri Gajanan Maharaj Shikshan Prasarak Mandal's Sharadchandra Pawar College of Pharmacy, At: Dumbarwadi, Post: Khamundi, Tal: Junnar, Dist: Pune – 410504, Maharashtra, India.<br>**DR. SHRIRAM RAMESH PETHAKAR**<br>Shramjivi Shikshan Prasarak Mandal's Shramjivi College of Pharmacy, Omerga, Dist: Osmanabad – 413606, Maharashtra, India.<br><br>hereby declare, |

<table>
<tr><td>2. Name, address and nationality of the joint applicant</td><td colspan="6">(i) that ~~I~~/We have not made any application for the same/substantially the same invention outside India.<br>Or<br>(ii) ~~that I/We who have made this application No……dated ……alone/jointly with……made for the same/substantially same invention, application(s) for patent in the other countries, the particulars of which are given below:~~</td></tr>
<tr><td>Name of the country</td><td>Date of application</td><td>Application No</td><td>Status of the application</td><td>Date of publication</td><td>Date of grant</td></tr>
<tr><td colspan="6">N/A</td></tr>
<tr><td>3. Name and address of the assignee</td><td colspan="6">(iii) that the rights in the application(s) have been assigned to ……<br>that I/~~We~~ undertake that upto the date of the grant of the patent by the Controller, I/~~We~~ would keep him informed in writing the details regarding corresponding applications for patents filed outside India within six months from the date of filing of such application.<br><br>Dated this 07th day of August 2021</td></tr>
<tr><td>4. To be signed by the applicant or his authorized patent agent</td><td colspan="6">Signature<br><br>Digitally signed by,</td></tr>
<tr><td>5. Name of the natural person who has signed</td><td colspan="6">VIJAYKUMAR SHIVPUJE<br>Sri Kripa, Akshay Nagar, Old Ausa Road, Latur, 413531, Maharashtra, India.</td></tr>
<tr><td></td><td colspan="6">To,<br>The Controller of Patents,<br>The Patent Office,<br>at…Mumbai…</td></tr>
<tr><td colspan="7">Note: - Strike out whichever is not applicable</td></tr>
</table>

| **FORM 1**<br>THE PATENTS ACT, 1970 (39 of 1970) and<br>THE PATENTS RULES, 2003<br>**APPLICATION FOR GRANT OF PATENT**<br>**(See section 7, 54 & 135 and sub-rule (1) of rule 20)** | **(FOR OFFICE USE ONLY)** |
|---|---|

| | | |
|---|---|---|
| | Application no: | |
| | Filing Date: | |
| | Amount of Fee Paid: | |
| | CBR No: | |
| | Signature: | |
| **1. APPLICANT'S REFERENCE/ IDENTIFICATION NO. (AS ALLOTTED BY OFFICE)** | | |

**2. TYPE OF APPLICATION [Please tick (✓) at the appropriate category]**

| Ordinary (✓) | | Convention ( ) | | PCT-NP ( ) | |
|---|---|---|---|---|---|
| Divisional ( ) | Patent of addition ( ) | Divisional ( ) | Patent of addition ( ) | Divisional ( ) | Patent of addition ( ) |

**3 A. APPLICANT (S)**

| **Name in full** | **Nationality** | **Country of residence** | **Address of the applicant** | |
|---|---|---|---|---|
| **DR. SHUBHRAJIT MANTRY** | Indian | India | House No. | Shri Gajanan Maharaj Shikshan Prasarak Mandal's Sharadchandra Pawar College of Pharmacy |
| | | | Street | At: Dumbarwadi, Post : Khamundi, Tal: Junnar |
| | | | City | Pune |
| | | | State | Maharashtra |
| | | | Country | India |
| | | | Pin Code | 410504 |
| **MISS. PALLAVI BHIMAJI** | Indian | India | House No. | Shri Gajanan Maharaj |

| | | | | |
|---|---|---|---|---|
| **GHOLAP** | | | | Shikshan Prasarak Mandal's Sharadchandra Pawar College of Pharmacy |
| | | | Street | At: Dumbarwadi, Post : Khamundi, Tal: Junnar |
| | | | City | Pune |
| | | | State | Maharashtra |
| | | | Country | India |
| | | | Pin Code | 410504 |
| **DR. SUMIT ASHOK JOSHI** | Indian | India | House No. | Shri Gajanan Maharaj Shikshan Prasarak Mandal's Sharadchandra Pawar College of Pharmacy |
| | | | Street | At: Dumbarwadi, Post : Khamundi, Tal: Junnar |
| | | | City | Pune |
| | | | State | Maharashtra |
| | | | Country | India |
| | | | Pin Code | 410504 |
| **DR. GANESH YOGIRAJ DAMA** | Indian | India | House No. | Shri Gajanan Maharaj Shikshan Prasarak Mandal's Sharadchandra Pawar College of Pharmacy |
| | | | Street | At: Dumbarwadi, Post : Khamundi, Tal: Junnar |
| | | | City | Pune |
| | | | State | Maharashtra |
| | | | Country | India |
| | | | Pin Code | 410504 |
| **DR. SHRIRAM RAMESH PETHAKAR** | Indian | India | House No. | Shramjivi Shikshan Prasarak Mandal's Shramjivi College of Pharmacy, Omerga |
| | | | Street | Omerga, Dist. Osmanabad |
| | | | City | Osmanabad |
| | | | State | Maharashtra |

| | | | | |
|---|---|---|---|---|
| | | | Country | India |
| | | | Pin Code | 413606 |

**3 B. CATEGORY OF APPLICANT [Please tick (✓) at the appropriate category]**

| Natural person (✓ ) | Other than natural person | | |
|---|---|---|---|
| | Small entity ( ) | Startup ( ) | Others ( ) |

**4. INVENTORS [Please tick (✓) at the appropriate category]**

| Are all the inventor(s) same as the applicant(s) named above? | Yes (✓) | No () |
|---|---|---|

**If "NO",** furnish the details of the inventor (s)

**5. TITLE OF THE INVENTION**

IMMEDIATE RELEASE TABLET OF ENALAPRIL MALEATE

| | | |
|---|---|---|
| **6. AUTHORISED REGISTERED PATENT AGENT (S)** | IN/PA No. | 1096 |
| | Name | VIJAYKUMAR SHIVPUJE |
| | Mobile No. | 09768665354 |
| **7. ADDRESS FOR SERVICE OF APPLICANT IN INDIA** | Name | MR. VIJAYKUMAR SHIVPUJE |
| | Postal address | Sri Kripa, Akshay Nagar, Old Ausa Road, Latur, 413531, Maharashtra, India. |
| | Telephone No. | NA |
| | Mobile no. | +91 9768665354 |
| | Fax No. | NA |
| | E-mail ID | vijay@patlex.in |

**8. IN CASE OF APPLICATION CLAIMING PRIORITY OF APPLICATION FILED IN CONVENTION COUNTRY, PARTICULARS OF CONVENTION APPLICATION**

| Country | Application Number | Filing date | Name of the applicant | Title of the invention | IPC (as classified in the convention country) |
|---|---|---|---|---|---|
| N/A | N/A | N/A | N/A | N/A | N/A |

**9. IN CASE OF PCT NATIONAL PHASE APPLICATION, PARTICULARS OF INTERNATIONAL APPLICATION FILED UNDER PATENT CO-OPERATION TREATY (PCT)**

| International application number | International filing date |
|---|---|
| N/A | N/A |

**10. IN CASE OF DIVISIONAL APPLICATION, FILED UNDER SECTION 16, PARTICULARS OF ORIGINAL (FIRST) APPLICATION**

| Original (first) application No. | Date of filing of original (first) application |
|---|---|
| N/A | N/A |

**11. IN CASE OF PATENT OF ADDITION, FILED UNDER SECTION 54, PARTICULARS OF MAIN APPLICATION OR PATENT**

| Main application/patent No. | Date of filing of main application |
|---|---|
| N/A | N/A |

**12. DECLARATIONS**

**(i) Declaration by the inventor (s)**

**(In case the applicant is an assignee:** the inventor(s) may sign herein below or the applicant may upload the assignment or enclose the assignment with this application for patent or send the assignment by post/electronic transmission duly authenticated within the prescribed period).

~~I~~/We, the above mentioned inventor(s) ~~is~~/are the true & first inventor(s) for this Invention and declare that the applicant(s) herein ~~is~~/are ~~my~~/our assignee or legal representative.

(a) Date: 07th August 2021

(b) Signature(s):

(c) Name(s): **DR. SHUBHRAJIT MANTRY** **MISS. PALLAVI BHIMAJI GHOLAP**

**DR. SUMIT ASHOK JOSHI** **DR. GANESH YOGIRAJ DAMA**

**DR. SHRIRAM RAMESH PETHAKAR**

**(ii) Declaration by the applicant(s) in the convention country N/A**

**(In case the applicant in India is different than the applicant in the convention country:** the applicant in the convention country may sign herein below or applicant in India may upload the assignment from the applicant in the convention country or enclose the said assignment with this application for patent or send the assignment by post/electronic transmission duly authenticated within the prescribed period).

I/We, the applicant(s) in the convention country declare that the applicant(s) herein is/are my/our assignee or legal representative.

(a) Date:

(b) Signature(s):

(c) Name(s) of the signatory

**(iii) Declaration by the applicant(s):**

**I/~~We~~, the applicant(s) hereby declare(s) that:-**

- ~~I am~~/ We are in possession of the above-mentioned invention.

○ The Complete/ ~~provisional~~ specification relating to the invention is filed with this application.

~~○ The invention as disclosed in the specification uses the biological material from India and the necessary permission from the competent authority shall be submitted by me/us before the grant of patent to me/us.~~

○ There is no lawful ground of objection to the grant of the patent to me/us.

○ ~~I am~~/ We are the true and first inventor(s).

○ ~~I am~~/ We are the assignee or legal representative of true & first inventors.

○ ~~The application or each of the applications, particulars of which are given in Paragraph-8 was the first application in convention country/countries in respect of my/our invention~~.

~~○ I/We claim the priority from the above mentioned application(s) filed in convention country/countries and state that no application for protection in respect of the invention had been made in a convention country before that date by me/us or by any person from which I/We derive the title.~~

~~○ My/Our application in India is based on international application under Patent Cooperation Treaty (PCT) as mentioned in Paragraph-9.~~

~~○ The application is divided out of my/our application particulars of which are given in Paragraph-10 and pray that this application may be treated as deemed to have been filed on _____ under section 16 of the Act.~~

~~○ The said invention is an improvement in/or modification of the invention particulars of which are given in Paragraph-11.~~

**13. FOLLOWING ARE THE ATTACHMENTS WITH THE APPLICATION**

(a) Form 2

| Item | Details | Fee | Remarks |
|---|---|---|---|
| Complete/ ~~provisional~~ specification)# | No. of pages (20) | 1600 | |
| No. of claim(s) | No, of claims (7) and no. of pages (2) | | |
| Abstract | No. of pages (**1**) | 0 | |
| No. of drawing(s) | No. of drawings (2) and No. of pages (1) | N/A | N/A |

# In case of a complete specification, if the applicant desires to adopt the drawings filed with his provisional specification as the drawings or part of the drawings for the complete specification under rule 13 (4), the number of such pages filed with the provisional specification are required to be mentioned here.

(b) ~~Complete specification (in conformation with the international application)/ as amended before the International Preliminary Examination Authority (IPEA) as applicable (2 copies).~~

(c) ~~Sequence listing in electronic form~~

(d) ~~Drawings (in conformation with the international application)/ as amended before the International Preliminary Examination Authority (IPEA), as applicable (2 copies).~~

(e) ~~Priority document(s) or a request to retrieve the priority document(s) from DAS (Digital Access Service)~~

~~if the applicant had already requested the office of first filing to make the priority document(s) available to DAS.~~

(f) ~~Translation of priority document/Specification/International Search Report/International Preliminary report on patentability.~~

(g) Statement and undertaking on Form 3

(h) Declaration of Inventorship on Form 5

(i) ~~Power of authority~~

(j)……

Total fee ☐ **1600** Rs. via e-payment.

~~I~~/We hereby declare that to the best of ~~my~~/our knowledge, information and belief the fact and matters slated herein are correct and ~~I~~/We request that a patent may be granted to me/us for the said invention.

Dated this 07th day of August 2021

Signature:

Name: **VIJAYKUMAR SHIVPUJE**

Sri Kripa, Akshay Nagar, Old Ausa Road, Latur, 413531, Maharashtra, India.

To,

The Controller of Patents

The Patent Office, at…**Mumbai**…

Note: -

* Repeat boxes in case of more than one entry.
* To be signed by the applicant(s) or by authorized registered patent agent otherwise where mentioned.
* Tick (✓)/ cross (x) whichever is applicable/ not applicable in paragraph-12.
* Name of the inventor and applicant should be given in full, family name in the beginning.
* Strike out the portion which is/are not applicable.
* For fee: See First Schedule;

# COMPLETE SPECIFICATION

DR. SHUBHRAJIT MANTRY
PALLAVI BHIMAJI GHOLAP
DR. SUMIT ASHOK JOSHI
DR. GANESH YOGIRAJ DAMA
DR. SHRIRAM RAMESH PETHAKAR

TOTAL SHEETS: 1
CURRENT SHEET: 1

**Figure 1**

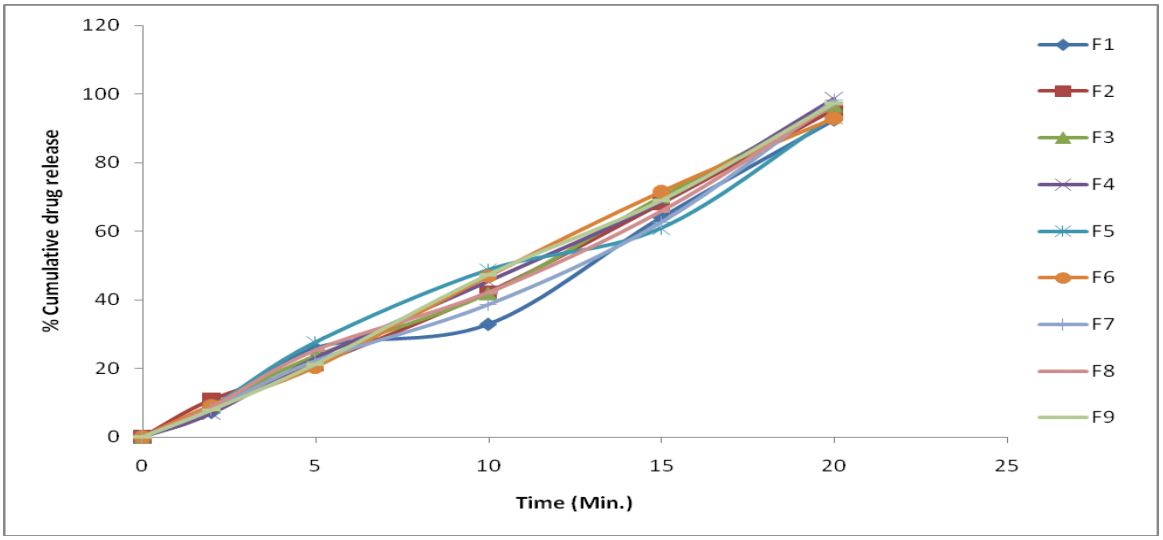
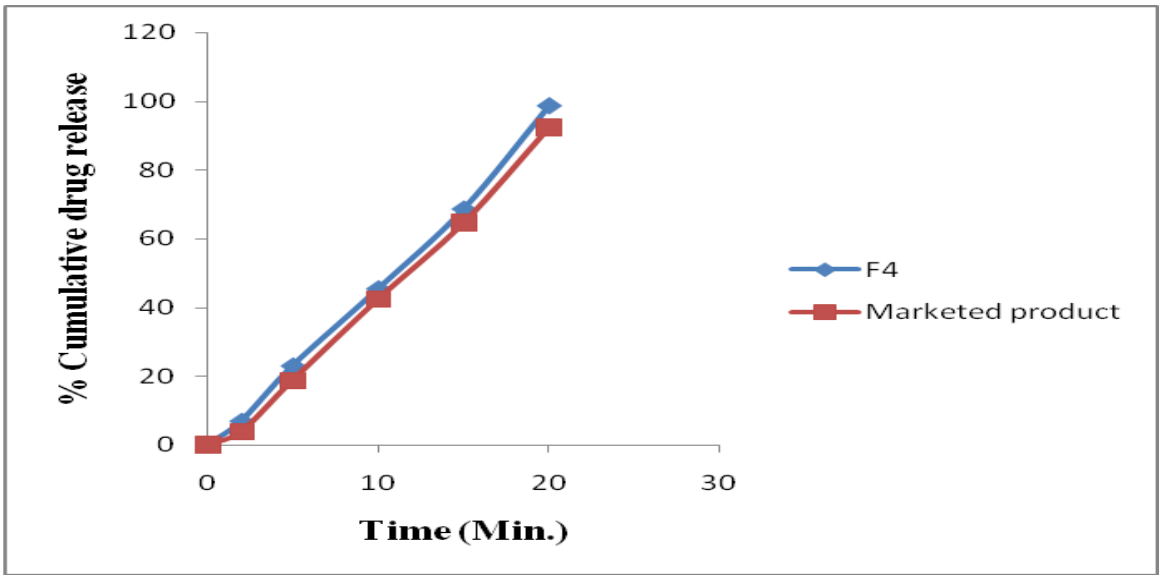



**Figure 2**




**Dated this 07th August 2021**

Digitally signed by,

**Vijaykumar Shivpuje,**
IN/PA 1096,
Sri Kripa, Akshay Nagar, Old Ausa Road, Latur, 413531, Maharashtra, India

**FORM 5**

**THE PATENTS ACT, 1970**

**(39 OF 1970) &**

**The Patents Rules, 2003**

**DECLARATION AS TO INVENTORSHIP**

**[See section 10 (6) and rule 13(6)]**

| | |
|---|---|
| **1. NAME OF THE APPLICANT (S)** | **DR. SHUBHRAJIT MANTRY**<br>**MISS. PALLAVI BHIMAJI GHOLAP**<br>**DR. SUMIT ASHOK JOSHI**<br>**DR. GANESH YOGIRAJ DAMA**<br>**DR. SHRIRAM RAMESH PETHAKAR** |

hereby declare that the true and first inventor(s) of the invention disclosed in the provisional specification filed in pursuance of ~~my~~/our application numbered _____ dated_____ ~~is~~/are **DR. SHUBHRAJIT MANTRY, MISS. PALLAVI BHIMAJI GHOLAP, DR. SUMIT ASHOK JOSHI, DR. GANESH YOGIRAJ DAMA** and **DR. SHRIRAM RAMESH PETHAKAR**

**2. INVENTORS**

**INVENTOR (1)**

**(a) NAME:** **DR. SHUBHRAJIT MANTRY**

**(B) NATIONALITY:** Indian

**(C) ADDRESS:** Shri Gajanan Maharaj Shikshan Prasarak Mandal's Sharadchandra Pawar College of Pharmacy, At: Dumbarwadi, Post: Khamundi, Tal: Junnar, Dist: Pune – 410504, Maharashtra, India.

Dated this 07th August 2021

Signature: -

Name of the signatory: - **DR. SHUBHRAJIT MANTRY**

**INVENTOR (2)**

**(a) NAME:** **MISS. PALLAVI BHIMAJI GHOLAP**

**(B) NATIONALITY:** Indian

**(C) ADDRESS:** Shri Gajanan Maharaj Shikshan Prasarak Mandal's Sharadchandra Pawar

College of Pharmacy, At: Dumbarwadi, Post: Khamundi, Tal: Junnar, Dist: Pune – 410504, Maharashtra, India.

Dated this 07th August 2021

Signature: -

Name of the signatory: - **MISS. PALLAVI BHIMAJI GHOLAP**

**INVENTOR (3)**

**(a) NAME:** **DR. SUMIT ASHOK JOSHI**

**(B) NATIONALITY:** Indian

**(C) ADDRESS:** Shri Gajanan Maharaj Shikshan Prasarak Mandal's Sharadchandra Pawar College of Pharmacy, At: Dumbarwadi, Post: Khamundi, Tal: Junnar, Dist: Pune – 410504, Maharashtra, India.

Dated this 07th August 2021

Signature: -

Name of the signatory: - **DR. SUMIT ASHOK JOSHI**

**INVENTOR (4)**

**(a) NAME:** **DR. GANESH YOGIRAJ DAMA**

**(B) NATIONALITY:** Indian

**(C) ADDRESS:** Shri Gajanan Maharaj Shikshan Prasarak Mandal's Sharadchandra Pawar College of Pharmacy, At: Dumbarwadi, Post: Khamundi, Tal: Junnar, Dist: Pune – 410504, Maharashtra, India.

Dated this 07th August 2021

Signature: -

Name of the signatory: - **DR. GANESH YOGIRAJ DAMA**

**INVENTOR (5)**

**(a) NAME:** **DR. SHRIRAM RAMESH PETHAKAR**

**(B) NATIONALITY:** Indian

**(C) ADDRESS:** Shramjivi Shikshan Prasarak Mandal's Shramjivi College of Pharmacy,

Omerga, Dist: Osmanabad – 413606, Maharashtra, India.

Dated this 07th August 2021

Signature: -

Name of the signatory: - **DR. SHRIRAM RAMESH PETHAKAR**

**3. DECLARATION TO BE GIVEN WHEN THE APPLICATION IN INDIA IS FILED BY THE APPLICANT(S) IN THE CONVENTION COUNTRY: -**

Not applicable.

**4. STATEMENT** (to be signed by the additional inventor(s) not mentioned in the application form)

~~I~~We assent to the invention referred to in the above declaration, being included in the complete specification filed in pursuance of the stated application.

Dated this August 2021.

Signature of the additional inventor(s) : -

Name: -

To, The Controller of Patent,
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**The Patent Act 1970**
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**COMPLETE SPECIFICATION**
**(see section 10 and rule 13)**

TITLE OF THE INVENTION

**IMMEDIATE RELEASE TABLET OF ENALAPRIL MALEATE**

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2. PREAMBLE TO THE DESCRIPTION

The following specification particularly describes the invention and the manner in which it is to be performed.

# IMMEDIATE RELEASE TABLET OF ENALAPRIL MALEATE

## FIELD OF THE INVENTION

The present invention is related to the field of Tablet formulation and more particularly to an immediate release tablet of Enalapril Maleate.

## BACKGROUND OF THE INVENTION

Among all dosage forms tablet is the most popular dosage form existing today because of its convenience of self administration, compactness and easy manufacturing; sometimes immediate onset of action is required than conventional therapy in many cases. So that to overcome these drawbacks, immediate release dosage form has emerged as alternative oral dosage forms.

Immediate release tablets are invented to disintegrate and release their dosage form with no special rate controlling features, such as special coatings and other techniques. Immediate release tablets are those which disintegrate swiftly and get dissolved to release the medicaments. Immediate release may be provided for by way of an appropriate pharmaceutically acceptable diluent or carrier, which diluent or carrier does not prolong, to an appreciable extent, the rate of drug release and/or absorption. This term excludes formulations which are adapted to provide for “modified”, “controlled”, “sustained”, “prolonged”, “extended” or “delayed” release of drug.

The immediate release tablets can be prepared by various methods such as Direct Compression, Wet granulation, Dry granulation by Roller compaction, Dry granulation by Slugging process and Mass-Extrusion. Direct Compression method is one of the simplest and cost effective method. The term “direct compression” is defined as the process by which tablets are compressed directly from powder mixture of API and suitable excipients. No pretreatment of the powder blend by wet or dry granulation procedure is required. It involves only blending and compression, thus

offering advantage particularly in terms of speedy production, as it requires fewer unit operations, less machinery, reduced number of personnel and considerably less processing time along with increased product stability.

Superdisintegrants are substances or a mixture of substances incorporated to the drug formulations, which assist dispersion or breakup of tablets and contents of capsules into smaller fragments for rapid dissolution. The objective behind the addition of disintegrant is to enlarge the surface area of the tablet fragments and to conquer cohesive forces that keep particles together in a tablet. When superdisintegrant contact with water they expand, swell, hydrate, dissolve, change volume or form and produce a disruptive transform in the tablet and rupture apart in the digestive, releasing the active ingredients for absorption.

Enalapril maleate belongs to the class of medicines called Angiotensin converting enzyme inhibitors (ACE inhibitors). It works by causing blood vessels to relax, lowering blood pressure and increasing the supply of blood and oxygen to the heart. Enalapril maleate Tablets are used To treat high blood pressure (hypertension), To treat symptomatic heart failure (weakening of heart function), It can lower the need to go to hospital and can help some patients live longer, to prevent signs of heart failure where the signs include shortness of breath, tiredness after light physical activity such as walking, or swelling of the ankles and feet and Prevention of Symptomatic Heart Failure in patients with Asymptomatic Left Ventricular Dysfunction (ejection fraction <35%).

Enalapril maleate is known to exist in 2 polymorphic modifications (forms I and II) with form II being the more thermodynamically stable form. Both forms exhibit similar solubilities, IR and Raman spectra, and differential scanning calorimetry thermograms. Enalapril is rapidly absorbed after oral administration of enalapril maleate, reaching peak plasma concentrations at about 1 hour. Enalapril Maleate is the maleate salt of enalapril, a dicarbocyl containing peptide and angiotensin converting enzyme (ACE)

inhibitor with antihypertensive activity. As a prodrug, enalapril is converted by de-estrification into its active form enalaprilat. Enalaprilat competitively binds to and inhibits ACE thereby blocking the conversion of angiotensin I to angiotensin II and result in vasodilation.

There are very few prior arts relating to immediate release formulation of Enalapril Maleate:

CN112494634A provides an oral preparation of enalapril maleate, which is characterized in that it comprises an immediate-release layer and a sustained-release layer; The quick-release layer includes enalapril maleate with a mass percentage of 2.5-6.25% of the total weight of the quick-release layer; The sustained-release layer includes enalapril maleate with a mass percentage of 3.5-6.25% of the total weight of the sustained-release layer.

CN105748422A provides a bilayer tablet comprising a pharmaceutical composition of an immediate release portion of enalapril and a sustained release portion of felodipine, characterized in that the bilayer tablet of the composition consists of a sustained release portion core, an immediate release portion core and any outer protective layer is selected, wherein the sustained release portion core contains felodipine, and the immediate release portion core contains enalapril or enalapril-acid addition salt.

CN102247366A provides a pharmaceutical composition comprising immediate-release pellets containing enalapril or enalapril-acid addition salts and sustained-release pellets containing felodipine is characterized in that it is prepared by mixing immediate release pellets containing enalapril or enalapril-acid addition salt, and then filling them into capsules in a certain proportion according to the results of the content determination.

The inventors of the present invention have prepared an immediate release tablet of Enalapril maleate providing disintegration time of 13 seconds and drug release of 98% in 20 minutes.

**OBJECTIVE OF THE INVENTION**

The main objective of the present invention is to provide an immediate release tablet of Enalapril maleate.

Yet another objective of the present invention is to provide a process of preparing an immediate release tablet of Enalapril maleate.

Yet another objective of the present invention is to provide an immediate release tablet of Enalapril maleate for lowering blood pressure and to treat symptomatic and asymptomatic left ventricular dysfunction.

**SUMMARY OF THE INVENTION**

Main embodiment of the present invention provides an immediate release tablet of Enalapril maleate comprising:

i. 10 mg of Enalapril maleate,
ii. 150 to 170 mg of Diluent,
iii. 1.5 to 16.5 mg of Superdisintegrant,
iv. 0.5 to 1.5 mg of Sweetner,
v. 18 to 22 mg of other pharmaceutical additives.

Another aspect of the present invention provides a process of preparing an immediate release tablet of Enalapril maleate by direct compression method.

Another aspect of the present invention provides an immediate release tablet of Enalapril maleate comprising:

i. 10 mg of Enalapril maleate,
ii. 150 to 170 mg of Microcrystalline cellulose,
iii. 1.5 to 16.5 mg of Crospovidone,

iv. 0.5 to 1.5 mg of Sodium Saccharin,

v. 9 to 11 mg of Magnesium Sterate,

vi. 9 to 11 mg of Talc.

Another aspect of the present invention provides an immediate release tablet of Enalapril maleate for lowering blood pressure and to treat symptomatic and asymptomatic left ventricular dysfunction.

**BRIEF DESCRIPTION OF DRAWINGS**

Figure 1: Percentage cumulative drug release of formulations F1-F9

Figure 2: Comparative cumulative drug release profile of formulations F4 with Marketed Product

**DESCRIPTION OF THE INVENTION**

The present invention is all about formulation of an immediate release tablet of Enalapril maleate and its method of preparation.

The term "comprising", which is synonymous with "including", "containing", or "characterized by" here is defined as being inclusive or open-ended, and does not exclude additional, unrecited elements or method steps, unless the context clearly requires otherwise.

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the invention pertains. The term "a" and "an" refers to one or to more than one (i.e., to at least one) of the grammatical object of the article. The information provided in this document, and particularly the specific details of the described exemplary aspects, is provided primarily for clearness of understanding and no unnecessary limitations are to be understood from there.

Although the invention has been described with reference to specific embodiments, this description is not meant to be construed in a limiting sense. Various modifications of the disclosed embodiments, as well as alternate embodiments of the invention, will become apparent to persons skilled in the art upon reference to the description of the invention. It is therefore contemplated that such modifications can be made without departing from the spirit or scope of the present invention as defined.

Main embodiment of the present invention provides an immediate release tablet of Enalapril maleate.

As per another preferred embodiment, the present invention provides an immediate release tablet of Enalapril maleate comprising:

i. 10 mg of Enalapril maleate,
ii. 150 to 170 mg of Diluent,
iii. 1.5 to 16.5 mg of Superdisintegrant,
iv. 0.5 to 1.5 mg of Sweetner,
v. 18 to 22 mg of other pharmaceutical additives.

As per another embodiment the active ingredient used is Enalapril Maleate which is the maleate salt form of Enalapril, a dicarbocyl containing peptide and angiotensin converting enzyme (ACE) inhibitor with antihypertensive activity.

As per another embodiment the Diluent is selected from Microcrystalline cellulose, Lactose, Low substituted Hydroxypropyl cellulose, starch, Mannitol.

As per another embodiment the Superdisintegrant is selected from Crosspovidone, Sodium Starch Glycolate, Crosscarmellose Sodium, Crosslinked Alginic acid, Calcium silicate, Crosslinked Polyvinylpyrrolidone.

As per another embodiment the Sweetner is selected from Sodium Saccharin, Saccharin, Dextrose, Fructose, Sorbitol, Mannitol, Sucrose, Xylitol.

As per another embodiment other pharmaceutical additives may include glidant, lubricant or antiadherents and is selected from Talc, Magnesium stearate, colloidal silicone dioxide, Sodium Stearyl Fumarate, Stearic acid.

As per another preferred embodiment, the present invention provides an immediate release tablet of Enalapril maleate comprising:

i. 10 mg of Enalapril maleate,
ii. 150 to 170 mg of Microcrystalline cellulose,
iii. 1.5 to 16.5 mg of Crospovidone,
iv. 0.5 to 1.5 mg of Sodium Saccharin,
v. 9 to 11 mg of Magnesium Sterate,
vi. 9 to 11 mg of Talc.

As per another embodiment, the present invention provides a process of preparing an immediate release tablet of Enalapril maleate by direct compression method comprising steps of:

a) Accurately weighing Enalapril Maleate, any one superdisintegrant, microcrystalline cellulose and passing through 60# mesh screen,
b) Mixing all the ingredients of step (a) for about 10 to 20 minutes to prepare a dry mix,
c) Accurately weighing magnesium stearate and talc separately and passing them through 60# mesh screen,
d) Mixing magnesium stearate and talc with the dry mix of step (b) for about 5 to 10 minutes to obtain powder blend,
e) Compressing the powder blend by using 8 mm diameter punch on a tablet machine to obtain immediate release tablet dosage form.

As per another embodiment, the present invention provides an immediate release tablet of Enalapril maleate for lowering blood pressure and to treat symptomatic and asymptomatic left ventricular dysfunction.

The invention is illustrated by the following examples which are not meant to restrict the scope of the invention in any manner.

**EXAMPLES**

**Example 1:** Process for preparing immediate release tablet of Enalapril maleate by direct compression method:

a) Enalapril Maleate, any one superdisintegrant and microcrystalline cellulose were weighed accurately and passed through 60# mesh screen,
b) All the ingredients of step (a) were mixed for about 10 to 20 minutes to prepare a dry mix,
c) Magnesium stearate and talc were separately weighed and passed them through 60# mesh screen,
d) Magnesium stearate and talc were mixed with the dry mix of step (b) for about 5 to 10 minutes to obtain powder blend,
e) The powder blend was compressed by using 8 mm diameter punch on a tablet machine to obtain immediate release tablet dosage form.

Table 1: Formula for Immediate Release Tablet

| **Ingredient** | **F1** | **F2** | **F3** | **F4** | **F5** | **F6** | **F7** | **F8** | **F9** |
|---|---|---|---|---|---|---|---|---|---|
| **Enalapril Maleate (mg)** | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| **Microcrystalline cellulose (mg)** | 160.8 | 156.8 | 152.8 | 163.8 | 161.8 | 159.8 | 166.8 | 165.8 | 164.8 |
| **Sodium Starch Glycolate (mg)** | 8 | 12 | 16 | - | - | - | - | - | - |
| **Crospovidone (mg)** | - | - | - | 5 | 7 | 9 | - | - | - |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Crosscarmellose Sodium (mg)** | - | - | - | - | - | - | 2 | 3 | 4 |
| **Sodium Saccharin (mg)** | 1.2 | 1.2 | 1.2 | 1.2 | 1.2 | 1.2 | 1.2 | 1.2 | 1.2 |
| **Magnesium Sterate (mg)** | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| **Talc (mg)** | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

**Example 2: Pre-compression Evaluation parameters of Powder Blend**

i. **Angle of repose** Angle of repose was determined using fixed funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and the angle of repose (θ) was calculated using the formula.

$$\theta = \tan^{-1}(h / r)$$

ii. **Bulk density** Bulk density was determined by pouring the blend into agraduated cylinder. The bulk volume (V) and weight ofthe powder (M) was determined. The bulk density wa scalculated by using the below mentioned formula,

Bulk density = Mass of powder/Bulk Volume of powder

iii. **Tapped density** The measuring cylinder containing a known mass of blend was tapped for a fixed time. The tapped density was calculated using the following formula,

Tapped density = Mass of powder / Tapped volume of powder

iv. **Compressibility index (C.I)** The simplest way for measurement of free flow of powder is compressibility, a indication of the ease with which a material can be induced to flow is given by compressibility index (I) which is calculated as follows,

C.I= (Tapped density-Bulk density/Tapped density) ×100

v. **Hausner's ratio** It is related to interparticle friction and could be used to predict powder flow property. Lower Hausner's ratio (<1.25) indicates better flow properties than higher ones (>1.25).

Hausner's ratio= Tapped density/ Bulk density

Table 2: Pre-compression Evaluation parameters of Powder Blend

| **Formulation code** | **Bulk density (gm/cm³)** | **Tapped density (gm/cm³)** | **Angle of repose (θ)** | **Percentage Compressibility (%)** | **Hausner's ratio** |
|---|---|---|---|---|---|
| F1 | 0.29 | 0.33 | 28.36 | 12.12 | 1.115 |
| F2 | 0.29 | 0.32 | 28.81 | 9.37 | 1.10 |
| F3 | 0.30 | 0.33 | 26.10 | 9.09 | 1.10 |
| F4 | 0.29 | 0.31 | 28.81 | 6.45 | 1.062 |
| F5 | 0.30 | 0.32 | 27.92 | 6.25 | 1.062 |
| F6 | 0.30 | 0.33 | 26.83 | 9.09 | 1.10 |
| F7 | 0.30 | 0.32 | 30.46 | 6.25 | 1.062 |
| F8 | 0.29 | 0.32 | 29.35 | 9.37 | 1.10 |
| F9 | 0.30 | 0.32 | 29.19 | 6.25 | 1.062 |

**Result:** The powder blend was evaluated for preformulation parameters and results are shown in Table 2.The angle of repose was in the range of 26.10˚ to 30.46˚ indicating the excellent flow properties. Bulk density was found in the range of 0.29 to 0.30 g/cm³ and the tapped density between 0.31 to 0.33 g/cm³.Hausners ratios was in the range of 1.062 to 1.115 indicating excellent flow ability. The Carr's compressibility index was found to be 6.25 to 12.12%. Hence prepared blend possessed excellent flow properties.

**Example 3: Evaluation of Immediate release tablet of Enalapril Maleate**

i. **Weight variation test**: Twenty tablets were selected randomly and average weight was determined. Then individual tablets were weighed and was compared with average weight. The comparison variation within the I.P limits, it passes the weight variation test.

ii. **Tablet hardness**: Tablet crushing strength or hardness, the force required to break a tablet in a diametric compression, was measured using Monsanto tablet hardness tester.

iii. **Thickness:** The thickness of individual tablets was measured using Vernier caliper, which permits accurate measurements and provides information of the variation between tablets.

iv. **Wetting time**: A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the paper and the time required for complete wetting was measured. The time required for water to reach upper surface of the tablet was noted as a wetting time.

Table 3: Evaluation of Enalapril Maleate immediate release tablets

| **Formulation code** | **Average Weight (mg)** | **Hardness ($kg/cm^2$) ± SD** | **Thickness (mm) ±SD** | **Wetting time (Sec) ± SD** |
|---|---|---|---|---|
| F1 | 199.33±1.154 | 3.4±0.157 | 2.7±0.196 | 45.37±1.172 |
| F2 | 200.4±1.000 | 3.5±0.105 | 2.7±0.185 | 52.20±1.705 |
| F3 | 199.3±1.000 | 3.4±0.101 | 2.5±0.115 | 48.12±1.437 |
| F4 | 200.22±1.537 | 3.6±0.152 | 2.7±0.208 | 41.10±1.427 |
| F5 | 196.2±1.527 | 3.6±0.105 | 2.6±0.152 | 57.21±0.724 |
| F6 | 193.45±1.527 | 3.4±0.110 | 2.5±0.102 | 55.20±1.311 |
| F7 | 199.15±1.723 | 3.6±0.115 | 2.7±0.208 | 52.45±1.225 |
| F8 | 201.00±1.000 | 3.5±0.086 | 2.7±0.102 | 56.40±0.735 |
| F9 | 198.17±1.154 | 3.6±0.057 | 2.5±0.115 | 52.60±2.636 |

**Result:** The compressed tablets were evaluated for physical properties and the results are tabulated in Table 3. The hardness of tablets was in the range of 3.43±0.10 to 3.60±0.156 $kg/cm^2$. The prepared tablets in all the

formulations have good mechanical strength. Mean and standard deviation of thickness was calculated. The thickness of tablets varies in between 2.5±0.10 to 2.7±0.208 mm. The friability of all formulations was found to be less than 1.0 % and was in the range of 90±0.005 to 95±0.051 % indicating a good mechanical resistance of tablets. Uniformity of weight of prepared tablets was found within specifications of Indian Pharmacopoeia. Uniformity of weight was found to be in the range of 193.66±1.527 to 210.33±1.527 mg.

v. **Water absorption ratio** : A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet of weight Wb was put on the paper and the time required for complete wetting was measured. The wetted tablet was then weighed (Wa). Water absorption ratio indicated with R, which was calculated by using the below mentioned equation.

$$R = 100 \times Wa\text{-}Wb/Wb$$

vi. **Tablet friability** : The friability of the tablets was measured in a Roche friabilator. Tablets of a known weight (W0) or a sample of 20 tablets were dedusted in a drum for a fixed time (100 revolutions) and weighed (W) again. Percentage friability was calculated from the loss in weight as given in equation as below. The weight loss should not be more than 1 %. Determination was made in triplicate.

$$\%Friability = Loss\ in\ weight/Initial\ weight \times 100$$

vii. **In-Vitro Disintegration time:** The test was carried out on 3 tablets using tablet disintegration tester of Electrolab, distilled water at 37°C ± 2°C was used as a disintegration media and the time in second taken for complete disintegration of the tablet with no palable mass remaining in the apparatus was measured in seconds.

viii. **Dissolution studies:** In Vitro dissolution studies for all the prepared tablets and the marketed available tablets was carried out using USP paddle method at 50 rpm in 900 ml of buffer solution (pH – 7.4) as dissolution media, maintained at 37 ± 0.5°. 5 ml of sample was

withdrawn from the dissolution medium at the specified regular intervals, filtered through Whattmann filter paper and assayed spectrophotometrically at 227 nm. An equal volume of pre-warmed (37°C) fresh medium was replaced into the dissolution medium after each sampling, to maintain the constant volume throughout the test. Then the cumulative percentage of drug release was calculated and represent graphically.

Table 4: Evaluation of Enalapril Maleate immediate release tablets

| **Formulation code** | **Water absorption ratio (%)** | **Friability (%)** | **In vitro disintegration time (Sec)** | **In vitro dissolution time (%)** | **Drug content uniformity (%)** |
|---|---|---|---|---|---|
| F1 | 90.47±0.446 | 0.69±0.055 | 25±1.154 | 92.47±1.062 | 94.52±1.100 |
| F2 | 95.56±0.845 | 0.75±0.026 | 21.12±1.402 | 95.53±1.001 | 95.74±1.112 |
| F3 | 80.95±0.783 | 0.50±0.062 | 19.62±2.823 | 96.51±0.654 | 97.32±0.456 |
| F4 | 100.98±0.258 | 0.68±0.075 | 13±3.185 | 98.64±1.217 | 98.94±0.321 |
| F5 | 81.81±0.569 | 0.45±0.041 | 15±1.571 | 93.33±0.472 | 95.20±1.526 |
| F6 | 90.98±0.631 | 0.55±0.051 | 18±2.968 | 93.00±0.358 | 95.58±0.651 |
| F7 | 100.20±0.473 | 0.59±0.040 | 20.77±2.251 | 98.20±1.046 | 98.65±0.774 |
| F8 | 95.45±0.685 | 0.69±0.005 | 19.20±2.323 | 96.96±1.282 | 98.52±0.661 |
| F9 | 90.47±0.661 | 0.49±0.228 | 16.44±2.401 | 97.22±0.103 | 98.49±1.121 |

Table 5: Dissolution profile at pH 7.4 phosphate buffer for Enalapril Maleate Immediate release Tablet

| Time (minutes) | F1 (%) | F2 (%) | F3 (%) | F4 (%) | F5 (%) | F6 (%) | F7 (%) | F8 (%) | F9 (%) |
|---|---|---|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 7.22 | 10.89 | 9.19 | 6.91 | 8.86 | 9.22 | 8.23 | 8.73 | 7.88 |
| 5 | 25.98 | 21.19 | 23.66 | 22.98 | 27.6 | 20.47 | 22.25 | 25.29 | 21.22 |
| 10 | 32.88 | 42.27 | 41.83 | 45.42 | 48.68 | 46.91 | 38.62 | 42.11 | 47.27 |
| 15 | 64 | 68.09 | 69.99 | 68.62 | 60.83 | 71.55 | 62.65 | 65.75 | 68.88 |
| 20 | 92.47 | 95.53 | 96.51 | 98.64 | 93.33 | 93 | 98.20 | 96.96 | 97.82 |

**Result:** All the batches of immediate release tablets for each formulation were found to disintegrate in less than 25±1.154 sec. F4 and F5 formulation showed minimum disintegration time 13±3.18 and 15±1.57 sec. respectively as compared to other formulations. The wetting time for all the formulated tablets was in the range 41.10±1.42 to 57.21±0.72 sec. F1 and F3 formulation showed minimum wetting time 45.37±1.17 and 48.12±1.43 sec. respectively as compared to other formulations. The water absorption ratio ranged from 80.95±0.783 to 100.98±0.258 %. The % drug content of tablets was checked in triplicate by UV spectrophotometer for all formulations. It was found to be between 94.52±1.100 to 98.94±0.321 %. In-vitro drug release of the prepared immediate release tablets was performed in pH 7.4 using USP type-II/IP-I dissolution apparatus. In-vitro drug release of all the formulations are as mentioned in the table 5. The results shows that the increase in proportion of superdisintegrants was associated with change in the overall cumulative drug release rate. In-vitro drug release of all the formulations were graphically represented by as shown in Figure 1. Among all the formulations, formulation F4 containing crospovidone as superdisintegrant exhibited excellent in-vitro

disintegration time and in vitro cumulative percentage drug release as compared to other formulations. Disintegration time of formulation F4 was found to be 13±3.185 seconds and the drug release was found to be 98.64±1.217% within 20 minutes. Therefore, the formulation F4 was considered as the best formulation.

**Example 4: Stability Studies**

The Immediate release tablets were packed in suitable packaging and stored under the following conditions for a period as prescribed by ICH guidelines for stability studies -40±2°C and RH 75%±5%. The tablets were withdrawn after 15, 30, 45, 60 and 90 days and evaluated hardness, disintegration time, drug content and drug release.

Table 6: Evaluation Parameter of Formulation F4 during Stability Study

| Time Interval (In Days) | Hardness(Kg /cm³) | Disintegration Time ( Sec) | Wetting Time(Sec) | Drug Content (%) | Drug Release (%) |
|---|---|---|---|---|---|
| 0 | 3.61±0.152 | 13±1.185 | 41.10±1.42 | 98.94±0.321 | 98.64±1.21 |
| 15 | 3.65±0.16 | 13.11±0.85 | 41.15±1.56 | 98.52±0.52 | 98.25±1.00 |
| 30 | 3.74±0.20 | 13.62±1.25 | 42.00±2.32 | 98.61±0.74 | 98.12±0.15 |
| 45 | 3.70±0.10 | 13.54±1.26 | 43.00±2.32 | 97.21±1.21 | 97.78±0.36 |
| 60 | 3.77±0.21 | 14.22±1.52 | 43.44±1.25 | 97.36±1.32 | 97.34±0.53 |
| 90 | 3.98±0.15 | 15.30±1.00 | 45.10±0.61 | 96.94±1.52 | 96.57±0.32 |

**Result:** The Table 6 shows the parameters of the tablets after stability study. The best formulations i.e. F4 was subjected to stability study by storing the formulations 40°C/75% RH up to 90 days. After 15, 30, 45, 60 and 90 days the tablets were evaluated for the hardness, disintegration time, wetting time, drug content and drug release. All the parameters were within the limits and complied the stability of the Tablets.

**Example 5: Comparative In-Vitro drug release profile with Marketed Formulation**

In-Vitro drug release profile of Optimized F4 batch of Immediate release Tablet of Enalapril maleate was done in comparison with Marketed Formulation and the dissolution profile was graphically represented as shown in Figure 2.

Table 7: Dissolution profile at pH 7.4 phosphate buffer for marketed product of Enalapril Maleate and Optimized F4 Immediate release Tablet

| TIME (minutes) | Marketed product (%) | Optimized Product (F4) |
|---|---|---|
| **0** | **0** | **0** |
| 2 | 3.9 | 6.91 |
| 5 | 18.76 | 22.98 |
| 10 | 42.42 | 45.42 |
| 15 | 64.67 | 68.62 |
| 20 | 92.45 | 98.64 |

**Result:** It can be observed that the % drug release of the Optimized F4 batch of Immediate release Tablet of Enalapril maleate was 98.64% as compared to 92.45% of marketed product therefore providing almost complete release of drug within 20 minutes of administration.

**We Claim,**

1. An immediate release tablet of Enalapril maleate comprising:
   i. 10 mg of Enalapril maleate,
   ii. 150 to 170 mg of Diluent,
   iii. 1.5 to 16.5 mg of Superdisintegrant,
   iv. 0.5 to 1.5 mg of Sweetner,
   v. 18 to 22 mg of other pharmaceutical additives.

2. The immediate release tablet of Enalapril maleate as claimed in claim 1 wherein the Diluent is selected from Microcrystalline cellulose, Lactose, Low substituted Hydroxypropyl cellulose, starch, Mannitol.

3. The immediate release tablet of Enalapril maleate as claimed in claim 1 wherein the Superdisintegrant is selected from Crosspovidone, Sodium Starch Glycolate, Crosscarmellose Sodium, Crosslinked Alginic acid, Calcium silicate, Crosslinked Polyvinylpyrrolidone.

4. The immediate release tablet of Enalapril maleate as claimed in claim 1 wherein the Sweetner is selected from Sodium Saccharin, Saccharin, Dextrose, Fructose, Sorbitol, Mannitol, Sucrose, Xylitol.

5. The immediate release tablet of Enalapril maleate as claimed in claim 1 wherein other pharmaceutical additives including glidant, lubricant or antiadherents is selected from Talc, Magnesium stearate, Colloidal silicone dioxide, Sodium Stearyl Fumarate, Stearic acid.

6. An immediate release tablet of Enalapril maleate comprising:
   i. 10 mg of Enalapril maleate,
   ii. 150 to 170 mg of Microcrystalline cellulose,
   iii. 1.5 to 16.5 mg of Crospovidone,
   iv. 0.5 to 1.5 mg of Sodium Saccharin,

v. 9 to 11 mg of Magnesium Sterate,

vi. 9 to 11 mg of Talc.

7. A process of preparing an immediate release tablet of Enalapril maleate by direct compression method comprising steps of:

a) Accurately weighing Enalapril Maleate, any one superdisintegrant, microcrystalline cellulose and passing through 60# mesh screen,

b) Mixing all the ingredients of step (a) for about 10 to 20 minutes to prepare a dry mix

c) Accurately weighing magnesium stearate and talc separately and passing them through 60# mesh screen,

d) Mixing magnesium stearate and talc with the dry mix of step (b) for about 5 to 10 minutes to obtain powder blend,

e) Compressing the powder blend by using 8 mm diameter punch on a tablet machine to obtain immediate release tablet dosage form.

**Dated this 07th August 2021**

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## ABSTRACT

### IMMEDIATE RELEASE TABLET OF ENALAPRIL MALEATE

The present invention is related to an immediate release tablet of Enalapril Maleate and the process of preparing the tablet by direct compression method. The present invention provides an immediate release tablet of Enalapril Maleate providing disintegration time of 13 seconds and drug release of 98% in 20 minutes for lowering blood pressure and to treat symptomatic and asymptomatic left ventricular dysfunction.

**FORM 9**

**THE PATENTS ACT, 1970**

**(39 OF 1970)**

**&**

**The Patents Rules, 2003**

**REQUEST FOR PUBLICATION**

**[See section 11A (2); rule 24A]**

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| 1. Name, address and Nationality of the applicant (s) | ~~I~~/ We<br>1. DR. SHUBHRAJIT MANTRY<br>2. MISS. PALLAVI BHIMAJI GHOLAP<br>3. DR. SUMIT ASHOK JOSHI<br>4. DR. GANESH YOGIRAJ DAMA<br>5. DR. SHRIRAM RAMESH PETHAKAR<br>hereby request for early publication of ~~my~~/our application for patent No. 202121035760 dated 2021/08/07 under section 11A(2) of the act. |

Dated this 8th day of September 2021.

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|---|---|
| 2. To be signed by the applicant or his authorized registered patent agent.<br><br>Name of the person who has signed | Digitally signed by,<br>**Agent for the Applicant**<br>Vijaykumar Shivpuje, IN/PA 1096, Sri Kripa, Akshay Nagar,<br>Old Ausa Road, Latur, 413531, Maharashtra, India.<br><br>To,<br>The Controller of Patents,<br>The Patent Office, At **Mumbai.** |