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

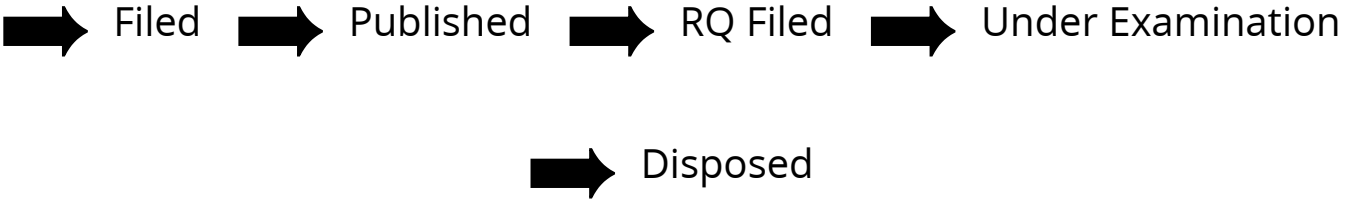
(http://ipindia.nic.in/index.htm)

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

Application Details	
APPLICATION NUMBER	202141039628
APPLICATION TYPE	ORDINARY APPLICATION
DATE OF FILING	01/09/2021
APPLICANT NAME	1 . DR. SRIKANTH 2 . DR. SHUBHRAJIT MANTRY 3 . DR. DIPANSU SAHU 4 . MR. TEJAS J. PATEL 5 . DR. SHRIRAM RAMESH PETHAKAR 6 . MRS. JYOTI BALAJI ARSUDE
TITLE OF INVENTION	PRONIOSOMAL GEL OF CELECOXIB
FIELD OF INVENTION	CHEMICAL
E-MAIL (As Per Record)	vijay@patlex.in
ADDITIONAL-EMAIL (As Per Record)	
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
(21) Application No.202141039628 A
(19) INDIA
(22) Date of filing of Application :01/09/2021
(43) Publication Date : 10/09/2021

(54) Title of the invention : PRONIOSOMAL GEL OF CELECOXIB

(51) International classification	:A61K0031415000, C07D0231120000, A61K0031635000, A61K0047140000, A61P0019020000
(31) Priority Document No	:NA
(32) Priority Date	:NA
(33) Name of priority country	:NA
(86) International Application No Filing Date	:PCT// :01/01/1900
(87) International Publication No	: NA
(61) Patent of Addition to Application Number Filing Date	:NA :NA
(62) Divisional to Application Number Filing Date	:NA :NA

(71)**Name of Applicant :**
1)DR. SRIKANTH
Address of Applicant :V. L. College of Pharmacy, Manik Prabhu Temple Road, Raichur 584103, Karnataka, India. Karnataka India
2)DR. SHUBHRAJIT MANTRY
3)DR. DIPANSU SAHU
4)MR. TEJAS J. PATEL
5)DR. SHRIRAM RAMESH PETHAKAR
6)MRS. JYOTI BALAJI ARSUDE
(72)**Name of Inventor :**
1)DR. SRIKANTH
2)DR. SHUBHRAJIT MANTRY
3)DR. DIPANSU SAHU
4)MR. TEJAS J. PATEL
5)DR. SHRIRAM RAMESH PETHAKAR
6)MRS. JYOTI BALAJI ARSUDE

(57) Abstract :
The present invention is related to Proniosomal gel of Celecoxib and its method of preparation. The said Proniosomal gel provides sustained release of the drug for over 24 hours therby enhancing biavailability of Celecoxib and is useful for treating Osteoarthritis.

No. of Pages : 30 No. of Claims : 7

भारतीय गैर न्यायिक

भारत INDIA

रु. 500

FIVE HUNDRED RUPEES

पाँच सौ रुपये

Rs. 500

सत्यमेव जयते

INDIA NON JUDICIAL

महाराष्ट्र MAHARASHTRA ◐ 2020 ◐ BC 700104

LATUR TREASURY
13 AUG 2021
Stamp H.C./Sr.Clerk

3211

...नोंदणी क्र. 30452 दि. 23/8/21

500

...नाव विजयकुमार काशिनाथ शिवपुजे

लातूर

व्हि. एन. केदार
प.क्र. 3701028 तहसिल समोर, लातूर

...घेणाऱ्याची सही

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

Power of Attorney by **DR. SRIKANTH, DR. SHUBHRAJIT MANTRY, DR. DIPANSU SAHU, MR. TEJAS J. PATEL, DR. SHRIRAM RAMESH PETHAKAR** and **MRS. JYOTI BALAJI ARSUDE** in the name of **VIJAYKUMAR KASHINATH 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. SRIKANTH	Indian	V. L. College of Pharmacy, Manik Prabhu Temple Road, Raichur – 584103, Karnataka, India.
DR. SHUBHRAJIT MANTRY	Indian	Sharadchandra Pawar College of Pharmacy, At: Dumbarwadi, Post: Khamundi, Tal: Junnar, Dist: Pune – 410504, Maharashtra, India.
DR. DIPANSU SAHU	Indian	Shree Naranjibhai Lalbhai Patel college of Pharmacy, Umrakh, Tq: Bardoli, Dist: Surat – 394345 Gujarat, India.
MR. TEJAS J. PATEL	Indian	Shree Naranjibhai Lalbhai Patel college of Pharmacy, Umrakh, Tq: Bardoli, Dist: Surat – 394345 Gujarat, India.
DR. SHRIRAM RAMESH PETHAKAR	Indian	Shramjivi Shikshan Prasarak Mandal's Shramjivi College of Pharmacy, Omerga, Dist: Osmanabad – 413606, Maharashtra, India.
MRS. JYOTI BALAJI ARSUDE	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 31st August 2021

Name	Signature
DR. SRIKANTH	
DR. SHUBHRAJIT MANTRY	
DR. DIPANSU SAHU	
MR. TEJAS J. PATEL	
DR. SHRIRAM RAMESH PETHAKAR	
MRS. JYOTI BALAJI ARSUDE	

To,

The Controller of Patent,

The Patent Office, at…**Chennai**…

FORM 3 **THE PATENTS ACT, 1970** **(39 OF 1970)** **and** **THE PATENTS RULES, 2003** **STATEMENT AND UNDERTAKING UNDER SECTION 8** **[See section 8, rule 12]**	
1. Name of the applicant (s),	~~I~~/We **DR. SRIKANTH** V. L. College of Pharmacy, Manik Prabhu Temple Road, Raichur – 584103, Karnataka, India. **DR. SHUBHRAJIT MANTRY** Sharadchandra Pawar College of Pharmacy, At: Dumbarwadi, Post: Khamundi, Tal: Junnar, Dist: Pune – 410504, Maharashtra, India. **DR. DIPANSU SAHU** Shree Naranjibhai Lalbhai Patel college of Pharmacy, Umrakh, Tq: Bardoli, Dist: Surat – 394345 Gujarat, India. **MR. TEJAS J. PATEL** Shree Naranjibhai Lalbhai Patel college of Pharmacy, Umrakh, Tq: Bardoli, Dist: Surat – 394345 Gujarat, India. **DR. SHRIRAM RAMESH PETHAKAR** Shramjivi Shikshan Prasarak Mandal's Shramjivi College of Pharmacy, Omerga, Dist: Osmanabad – 413606, Maharashtra, India. **MRS. JYOTI BALAJI ARSUDE** Shramjivi Shikshan Prasarak Mandal's Shramjivi College of Pharmacy, Omerga, Dist: Osmanabad – 413606, Maharashtra, India. hereby declare,

<table>
<tr><td>2. Name, address and nationality of the joint applicant</td><td colspan="5">(i) that ~~I~~/We have not made any application for the same/substantially the same invention outside India.
Or
(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="5">(iii) that the rights in the application(s) have been assigned to ……
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.

Dated this 1st day of September 2021</td></tr>
<tr><td>4. To be signed by the applicant or his authorized patent agent</td><td colspan="5">Signature

Digitally signed by,</td></tr>
<tr><td>5. Name of the natural person who has signed</td><td colspan="5">VIJAYKUMAR SHIVPUJE
Sri Kripa, Akshay Nagar, Old Ausa Road, Latur, 413531, Maharashtra, India.</td></tr>
<tr><td></td><td colspan="5">To,
The Controller of Patents,
The Patent Office,
at…Chennai…</td></tr>
<tr><td colspan="6">Note: - Strike out whichever is not applicable</td></tr>
</table>

FORM 1 THE PATENTS ACT, 1970 (39 of 1970) and THE PATENTS RULES, 2003 **APPLICATION FOR GRANT OF PATENT** **(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. SRIKANTH	Indian	India	House No.	V. L. College of Pharmacy
			Street	Manik Prabhu Temple Road, Raichur
			City	Raichur
			State	Karnataka
			Country	India
			Pin Code	584103
DR. SHUBHRAJIT MANTRY	Indian	India	House No.	Sharadchandra Pawar College of Pharmacy
			Street	At: Dumbarwadi, Post : Khamundi, Tal: Junnar

			City	Pune
			State	Maharashtra
			Country	India
			Pin Code	410504
DR. DIPANSU SAHU	Indian	India	House No.	Shree Naranjibhai Lalbhai Patel college of Pharmacy
			Street	Umrakh, Tal: Bardoli, Dist: Surat
			City	Surat
			State	Gujarat
			Country	India
			Pin Code	394345
MR. TEJAS J. PATEL	Indian	India	House No.	Shree Naranjibhai Lalbhai Patel college of Pharmacy
			Street	Umrakh, Tal: Bardoli, Dist: Surat
			City	Surat
			State	Gujarat
			Country	India
			Pin Code	394345
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
MRS. JYOTI BALAJI ARSUDE	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

PRONIOSOMAL GEL OF CELECOXIB

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: 1St September 2021

(b) Signature(s):

(c) Name(s): **DR. SRIKANTH** **DR. SHUBHRAJIT MANTRY**

DR. DIPANSU SAHU **MR. TEJAS J. PATEL**

DR. SHRIRAM RAMESH PETHAKAR **MRS. JYOTI BALAJI ARSUDE**

(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 (24)	1600	
No. of claim(s)	No, of claims (7) and no. of pages (1)		
Abstract	No. of pages (1)	0	
No. of drawing(s)	No. of drawings (8) and No. of pages (4)	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 1st day of September 2021

Signature:

Name: **MR. VIJAYKUMAR SHIVPUJE**

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

To,

The Controller of Patents

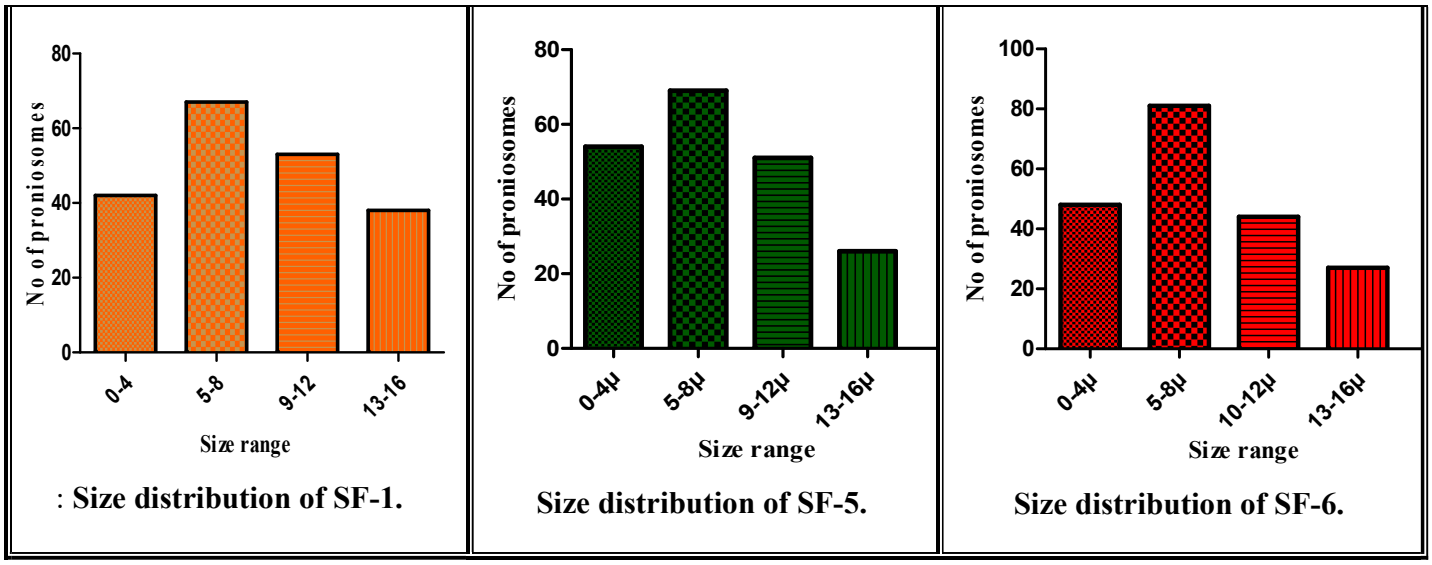
The Patent Office, at…**Chennai**…

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. SRIKANTH
DR. SHUBHRAJIT MANTRY
DR. DIPANSU SAHU
TEJAS PATEL
SHRIRAM RAMESH PETHAKAR
JYOTI BALAJI ARSUDE

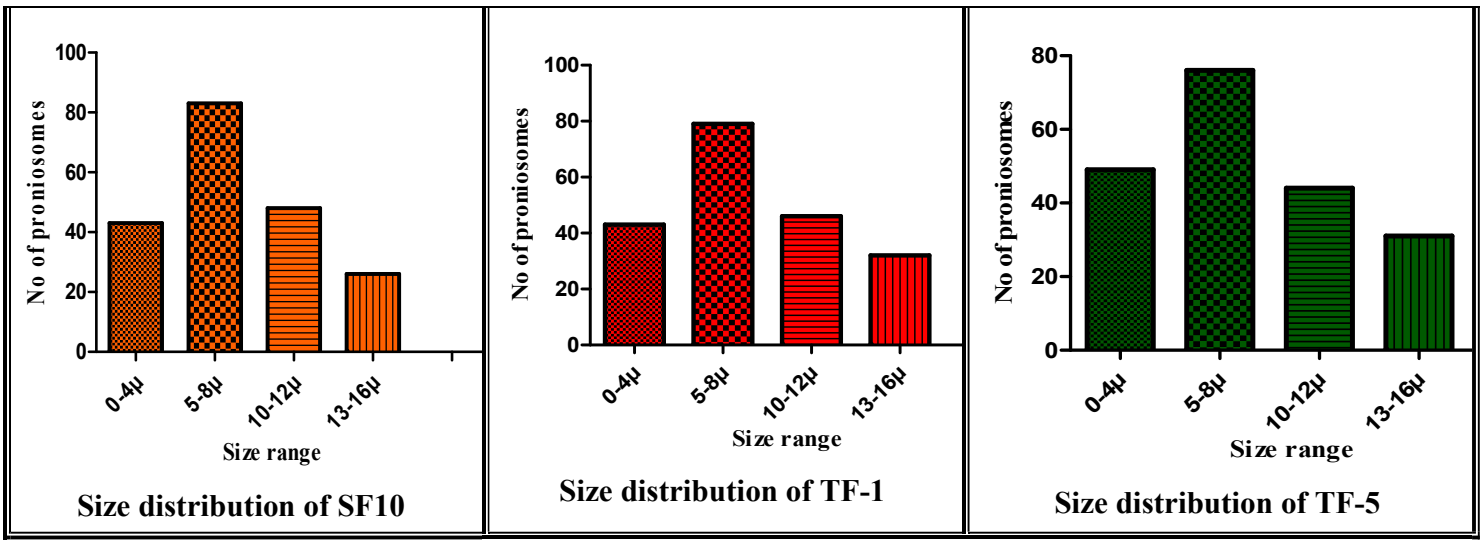


: Size distribution of SF-1.

Size distribution of SF-5.

Size distribution of SF-6.

Figure 1



Size distribution of SF10

Size distribution of TF-1

Size distribution of TF-5

Figure 2

Dated this 01st September 2021

Digitally signed by,

Vijaykumar Shivpuje,

IN/PA 1096,

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

DR. SRIKANTH
DR. SHUBHRAJIT MANTRY
DR. DIPANSU SAHU
TEJAS PATEL
SHRIRAM RAMESH PETHAKAR
JYOTI BALAJI ARSUDE

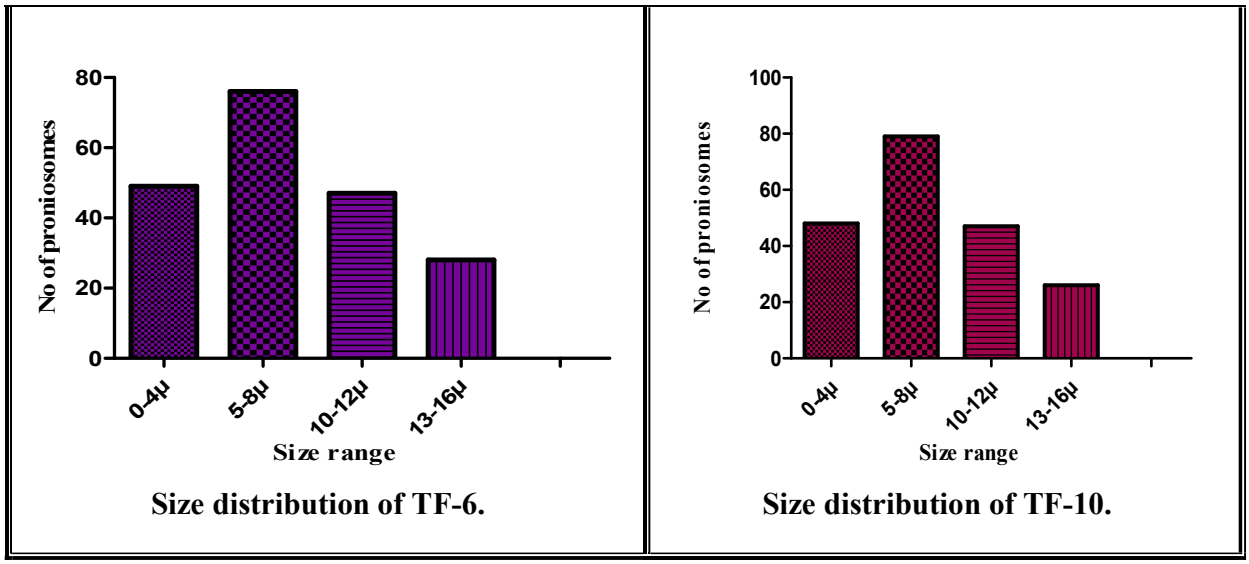


Figure 3

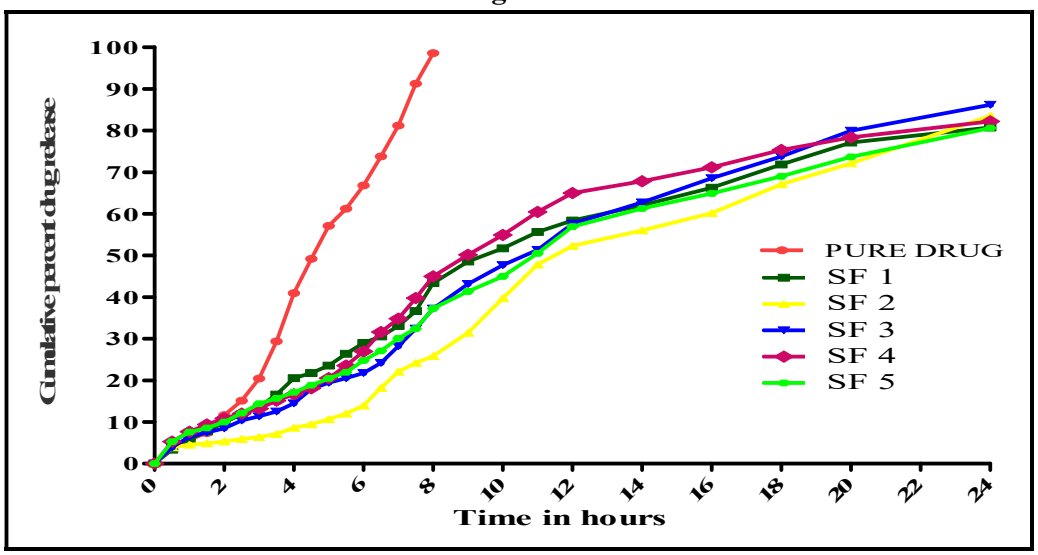


Figure 4

Dated this 01st September 2021

Digitally signed by,

Vijaykumar Shivpuje,

IN/PA 1096,

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

DR. SRIKANTH
DR. SHUBHRAJIT MANTRY
DR. DIPANSU SAHU
TEJAS PATEL
SHRIRAM RAMESH PETHAKAR
JYOTI BALAJI ARSUDE

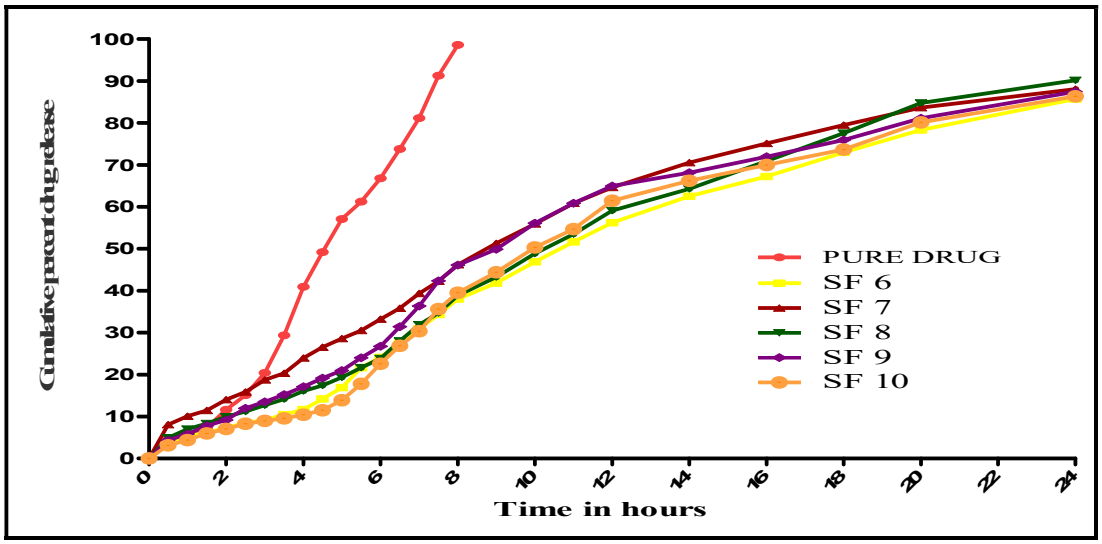


Figure 5

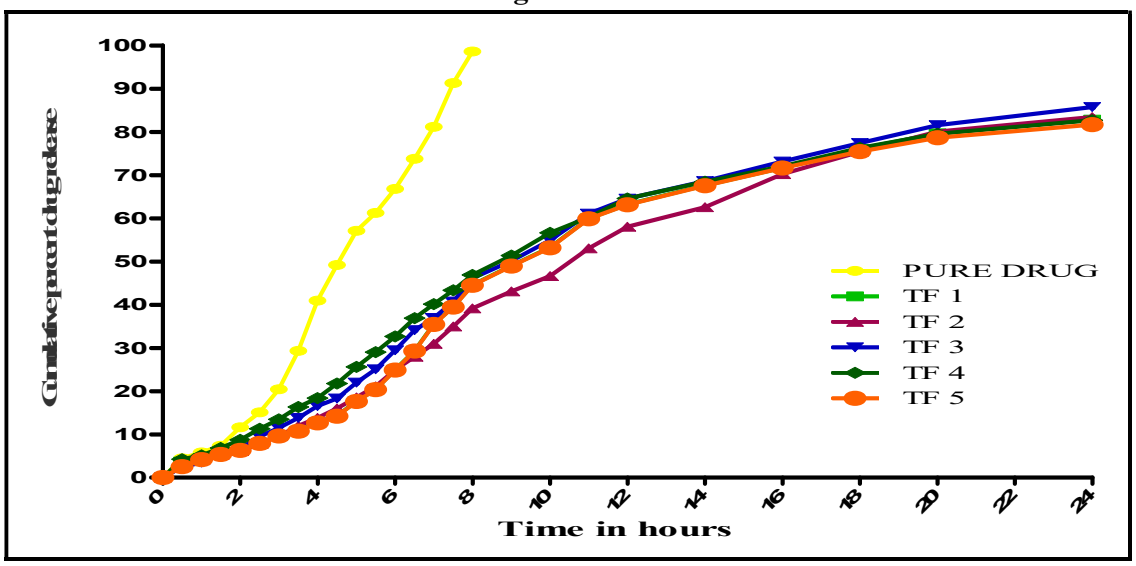


Figure 6

Dated this 01st September 2021

Digitally signed by,

Vijaykumar Shivpuje,

IN/PA 1096,

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

COMPLETE SPECIFICATION

DR. SRIKANTH
DR. SHUBHRAJIT MANTRY
DR. DIPANSU SAHU
TEJAS PATEL
SHRIRAM RAMESH PETHAKAR
JYOTI BALAJI ARSUDE

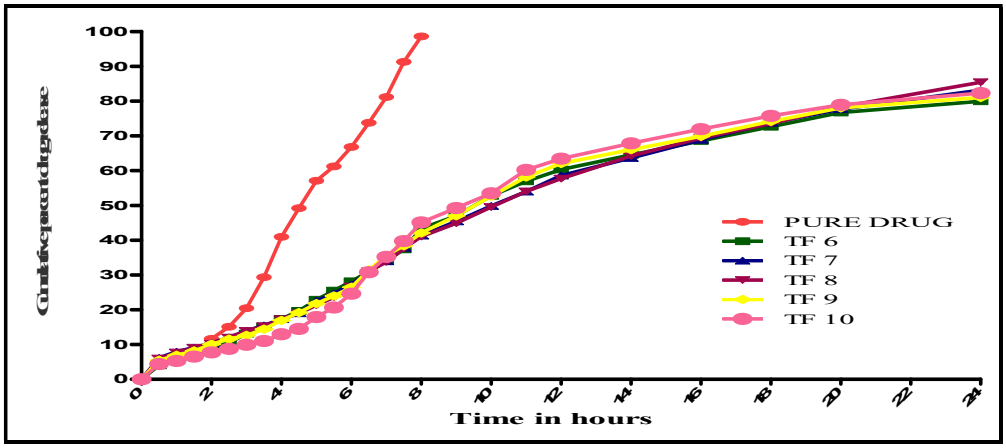


Figure 7

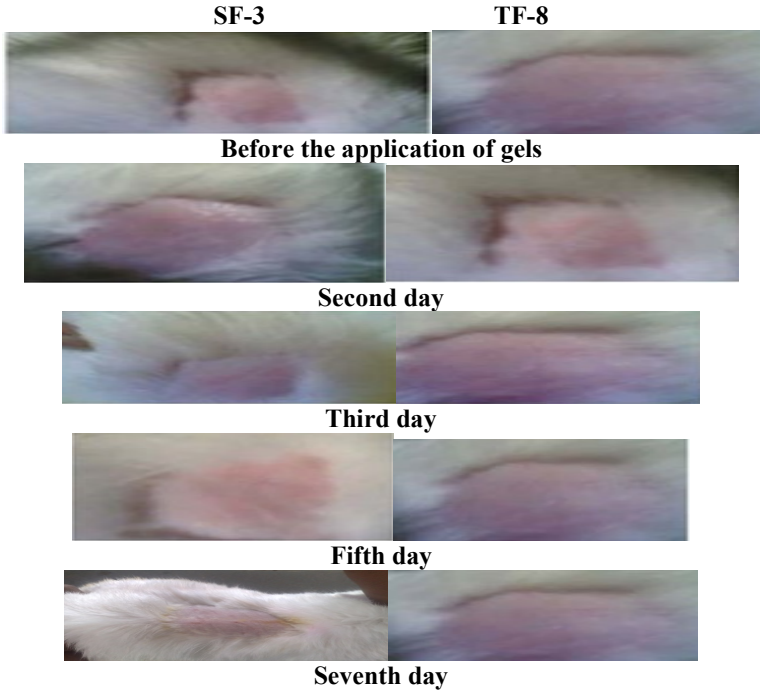


Figure 8

Dated this 01st September 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. SRIKANTH** **DR. SHUBHRAJIT MANTRY** **DR. DIPANSU SAHU** **MR. TEJAS J. PATEL** **DR. SHRIRAM RAMESH PETHAKAR** **MRS. JYOTI BALAJI ARSUDE**

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. SRIKANTH, DR. SHUBHRAJIT MANTRY, DR. DIPANSU SAHU, MR. TEJAS J. PATEL, DR. SHRIRAM RAMESH PETHAKAR** and **MRS. JYOTI BALAJI ARSUDE.**

2. INVENTORS

INVENTOR (1)

(a) NAME: **DR. SRIKANTH**

(B) NATIONALITY: Indian

(C) ADDRESS: V. L. College of Pharmacy, Manik Prabhu Temple Road, Raichur – 584103, Karnataka, India

Dated this 1st September 2021

Signature: -

Name of the signatory: - **DR. SRIKANTH**

INVENTOR (2)

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

(B) NATIONALITY: Indian

(C) ADDRESS: Sharadchandra Pawar College of Pharmacy, At: Dumbarwadi,

Post: Khamundi, Tal: Junnar, Dist: Pune – 410504,
Maharashtra, India.

Dated this 1st September 2021

Signature: -

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

INVENTOR (3)

(a) NAME: **DR. DIPANSU SAHU**

(B) NATIONALITY: Indian

(C) ADDRESS: Shree Naranjibhai Lalbhai Patel college of Pharmacy, Umrakh,
Tal: Bardoli, Dist: Surat – 394345 Gujarat, India.

Dated this 1st September 2021

Signature: -

Name of the signatory: - **DR. DIPANSU SAHU**

INVENTOR (4)

(a) NAME: **MR. TEJAS J. PATEL**

(B) NATIONALITY: Indian

(C) ADDRESS: Shree Naranjibhai Lalbhai Patel college of Pharmacy, Umrakh,
Tal: Bardoli, Dist: Surat – 394345 Gujarat, India.

Dated this 1st September 2021

Signature: -

Name of the signatory: - **MR. TEJAS J. PATEL**

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 1st September 2021

Signature: -

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

INVENTOR (6)

(a) NAME: **MRS. JYOTI BALAJI ARSUDE**

(B) NATIONALITY: Indian

(C) ADDRESS: Shramjivi Shikshan Prasarak Mandal's Shramjivi College of Pharmacy,
Omerga, Dist: Osmanabad – 413606, Maharashtra, India.

Dated this 1st September 2021

Signature: -

Name of the signatory: - **MRS. JYOTI BALAJI ARSUDE**

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 1st September 2021.

Signature of the additional inventor(s) : -

Name: -

To, The Controller of Patent,
The Patent Office, at…**Chennai**…

Form 2
The Patent Act 1970
(39 of 1970)
&
The Patent Rules, 2003
COMPLETE SPECIFICATION
(see section 10 and rule 13)

TITLE OF THE INVENTION: **PRONIOSOMAL GEL OF CELECOXIB**

1. APPLICANT(S)

(a) NAME: DR. SRIKANTH
NATIONALITY: Indian
ADDRESS: V. L. College of Pharmacy, Manik Prabhu Temple Road, Raichur – 584103, Karnataka, India.

(b) NAME: DR. SHUBHRAJIT MANTRY
NATIONALITY: Indian
ADDRESS: Sharadchandra Pawar College of Pharmacy, At: Dumbarwadi, Post: Khamundi, Tal: Junnar, Dist: Pune – 410504, Maharashtra, India.

(c) NAME: DR. DIPANSU SAHU
NATIONALITY: Indian
ADDRESS: Shree Naranjibhai Lalbhai Patel college of Pharmacy, Umrakh, Tq: Bardoli, Dist: Surat – 394345 Gujarat, India.

(d) NAME: MR. TEJAS PATEL
NATIONALITY: Indian
ADDRESS: Shree Naranjibhai Lalbhai Patel college of Pharmacy, Umrakh, Tq: Bardoli, Dist: Surat – 394345 Gujarat, India.

(e) NAME: DR. SHRIRAM RAMESH PETHAKAR
NATIONALITY: Indian
ADDRESS: Shramjivi Shikshan Prasarak Mandal's Shramjivi College of Pharmacy, Omerga, Dist: Osmanabad – 413606, Maharashtra, India.

(f) NAME: MRS. JYOTI BALAJI ARSUDE
NATIONALITY: Indian
ADDRESS: Shramjivi Shikshan Prasarak Mandal's Shramjivi College of Pharmacy, Omerga, Dist: Osmanabad – 413606, Maharashtra, India.

2. PREAMBLE TO THE DESCRIPTION

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

PRONIOSOMAL GEL OF CELECOXIB

FIELD OF THE INVENTION

The present invention is related to the field of Transdermal drug delivery system and more particularly to proniosomal gel of CELECOXIB.

BACKGROUND OF THE INVENTION

Novel drug delivery systems (NDDS) provide control of drug release in the body, which is either of temporal or spatial nature or both. It attempts to either sustain drug action at a predetermined rate or maintains a relatively constant, effective drug level in the body with concomitant minimization of undesirable side effects. . It also localizes drug action by spatial placement of control release systems adjacent to or in the diseased tissue or organ or target drug action by using carriers or chemical derivatization to deliver drug to particular target cell type. It is difficult to find the ideal novel drug delivery systems, but many attempts have been made to achieve through novel approaches in drug delivery. The most common form of delivery of drugs is the oral route, but it still faces challenges by other delivery systems in terms of patient compliance, therapeutic efficacy and safety. A number of novel drug delivery systems have emerged encompassing various routes of administration, to achieve controlled and targeted drug delivery. Transdermal drug delivery systems are self contained discrete dosage forms which when applied to the intact skin deliver the drug through the skin at a controlled rate to the systemic circulation. In recent years, vesicles have become the vehicle of choice in drug delivery as they were found to be of value in immunology, membrane biology, diagnostic techniques and genetic engineering. Vesicles can play a significant role in modeling biological membranes in the transport and targeting of active agents. Encapsulation of a drug in vesicular structures can be predicted to prolong the existence of the drug in systemic circulation and reduces the toxicity if selective uptake can be achieved.

Vesicular drug delivery reduces the cost of therapy by improved bioavailability of medication, especially in case of poorly soluble drugs and can incorporate both hydrophilic and lipophilic drugs. These systems delay drug elimination of rapidly metabolizing drugs and function as sustained release systems and solve the problems of drug insolubility, instability and rapid degradation. Consequently, a number of vesicular delivery systems such as liposomes, transferosomes, pharmacosomes, niosomes/proniosomes etc., were developed. However, the lipid bilayers in the stratum corneum are recognized as the rate limiting barrier for the penetration of drugs through the skin. Vesicular systems such as niosomes are considered very promising to overcome this permeation barrier of skin. They may act as penetration enhancers or even as vehicles for bioactive materials. Furthermore, they can be used as controlled percutaneous drug delivery vehicles. The applicability of these vesicular systems is, however, limited because of their stability problems. To overcome the limitations of vesicular drug delivery, provesicular approach was introduced in which a dry product or a liquid crystalline gel that could be hydrated immediately before use and would avoid many of the problems associated with niosomal dispersion and problems of physical stability.

Proniosomes are vesicular systems, in which the vesicles are made up of nonionic based surfactants, cholesterol and other additives. Semisolid liquid crystal gel (proniosomes) prepared by dissolving the surfactant in a minimal amount of an acceptable solvent, namely ethanol and then hydration with least amount of water to form a gel. These structures are liquid crystalline compact niosomes hybrids that can be converted into niosomes immediately upon hydration and are used as topical/transdermal applications. Use of proniosomal gel in topical/dermal delivery does not require hydration prior to application, but they can be applied as such or loaded on a base material of emulsion, gel, ointment etc., prior to application. The base material helps in the application of the formulation to the skin and dilution of the active material. Proniosomes are nowadays used to enhance drug delivery in addition to conventional niosomes. They

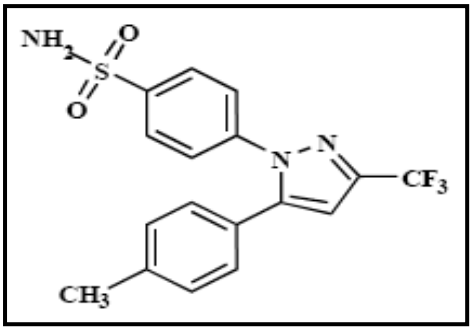
are becoming popular due to their semisolid/liquid crystalline compact nature when compared to niosome dispersion. Proniosomal gels generally appears as transparent, translucent or white semisolid gel, which makes them physically stable during storage and transport. The beauty of these proniosomes lies in their ability to rearrange as stable niosomal suspensions on hydration with water.

Proniosomes are microscopic lamellar structures, hexangular structures, and blockish structures and their location is clear, semitransparent, and semi-solid gel-like structures. Consistent with their methodology of preparation, Proniosomes are unilamellar or multi-lamellar. They even have bilayer in their structure having hydrophilic ends that are exposed on the surface and hydrophobic chains face one another within the bilayer inside the vesicles. Bilayer consists of non-ionic surface-active agents. To create a bilayer surfactant molecule, offer direction in such a method that hydrophilic ends of the non-ionic surfactant are arranged toward the outside, whereas the hydrophobic ends exist within the opposite direction. Hydrophilic drugs are placed at intervals in the area encircled within the vesicle and also the hydrophobic medication is implanted within the bilayer. For association, in liquid media Proniosomes attach to cholesterol with different categories of non-ionic surfactant like alkyl radical or dialkyl polyglycerol ether.

Proniosomes are dry formulation of water soluble carrier particles that are coated with surfactant. They are rehydrated to form niosomal dispersion immediately before use on agitation in hot aqueous media within minutes. Proniosomes are physically stable during the storage and transport. Drug encapsulated in the vesicular structure of proniosomes prolong the existence of drug in the systematic circulation and enhances the penetration into target tissue and reduce toxicity. From a technical point of view, niosomes are promising drug carriers as they possess greater chemical stability and lack of many disadvantages associated with

liposomes, such as high- cost and variable purity problems of phospholipids.

Celecoxib is a nonsteroidal anti-inflammatory drug (NSAID) able to selectively inhibit COX-2 activity and exhibits antiinflammatory, analgesic and antipyretic activities. It has been used in the treatment of rheumatoid arthritis, osteoarthritis, acute pain. It is pale yellowish white solid having 158^0C melting point. It is sparingly soluble in water and very soluble in methanol, ethanol and 2% SLS buffer. Celecoxib belongs to class II under BCS and exhibit low and variable oral bioavailability due to its poor aqueous solubility.



Chemical name of Celecoxib is 4-[5-(4-methylphenyl)-3- (trifluoromethyl) pyrazol-1-yl] benzene sulphonamide. The Molecular formula of Celecoxib is C17H14F3N3O2S and Molecular weight is 381.373 gm/mol. Celecoxib exhibits 97% protein binding and half life of 7.8-13 hours. Celecoxib is a highly selective inhibitor of the COX-2 isoform of cyclooxygenase, inhibits the transformation of arachidonic acid to prostaglandin precursors. Celecoxib is approximately 10-20 times more selective for COX-2 inhibition over COX-1. It binds with its polar sulfonamide side chain to a hydrophilic side pocket region close to the active COX-2 binding site. Serious adverse drug reactions include: cardiovascular thrombotic events, myocardial infarction, stroke; Bleeding, ulceration and perforation of the stomach or intestines; Chest pain, weakness, shortness of breath, slurred speech, problems with vision or balance; Black, bloody, coughing up blood or vomit that looks like coffee grounds and swelling or rapid weight gain.

Celecoxib is mainly indicated for Osteoarthritis, rheumatoid arthritis, juvenile rheumatoid arthritis, ankylosing spondylitis, acute pain and primary dysmenorrhea in the dose range of 50- 200 mg daily. The reasons for incorporating the celecoxib into proniosomal drug delivery system is to overcome the problems of extensively bounding to plasma proteins, short biological half-life and low and variable oral bioavailability. Some of the advantages of Proniosomal gel are:

1. Provides controlled and sustained release of drugs.
2. Provides greater physical and chemical stability
3. Easy for transportation, distribution, storage, and dosing.
4. Degradation by hydrolysis or oxidation problems is avoided.
5. No special conditions required for storage and handling.
6. Avoid stability problems like fusion, aggregation, sedimentation and leakage on storage.
7. Uses acceptable solvents in minimum quantity in the preparation.
8. Proniosomes have the potential for entrapping a wide range of drugs
9. Provides targeted and sustained release due to depot formation and achieves localized drug action.
10. Easy to use as they can be hydrated just before use.
11. Improve bioavailability of poorly water soluble drugs

The inventors of the present invention have prepared a novel vesicular based formulation known as Proniosomal gel of Celecoxib which provides sustained release of the drug for over 24 hours with enhanced biavailability and reduction in side effects as compared to conventional dosage form such as talets and capsules. The detailed invention is decribed as herein.

OBJECTIVE OF THE INVENTION

The main objective of the present invention is to provide Proniosomal gel of Celecoxib.

Yet another objective of the present invention is to provide a process of preparing Proniosomal gel of Celecoxib.

Yet another objective of the present invention is to provide Proniosomal gel of Celecoxib for treating Osteoarthritis, rheumatoid arthritis, juvenile rheumatoid arthritis, ankylosing spondylitis, acute pain and primary dysmenorrhea.

SUMMARY OF THE INVENTION

Main embodiment of the present invention provides Proniosomal gel of Celecoxib.

Another aspect of the present invention provides Proniosomal gel of Celecoxib comprising:

i. Celecoxib,
ii. Lecithin,
iii. Cholesterol,
iv. Surfactant,
v. Polyacrylic acid

wherin ratio of Surfactant: Cholesterol is from 5:5 to 9:1.

Another aspect of the present invention provides a process of preparing Proniosomal gel of Celecoxib by coacervation phase separation method.

Another aspect of the present invention provides Proniosomal gel of Celecoxib for treating Osteoarthritis, rheumatoid arthritis, juvenile rheumatoid arthritis, ankylosing spondylitis, acute pain and primary dysmenorrhea.

BRIEF DESCRIPTION OF DRAWINGS

Figure 1: Particle size distribution SF-1, SF-5 and SF-6 Batch
Figure 2: Particle size distribution of SF- 10, TF-1 and TF-5 Batch
Figure 3: Particle size distribution of TF-6 and TF-10 Batch
Figure 4: Comparison of dissolution profile of batches SF-1, SF-2, SF-3, SF-4 and SF-5 formulations with pure drug

Figure 5: Comparison of dissolution profile of batches SF-6, SF-7, SF-8, SF-9 and SF-10 formulations with pure drug.

Figure 6: Comparison of dissolution profile of batches TF-1, TF-2, TF-3, TF-4 and TF-5 formulations with pure drug.

Figure 7: Comparison of dissolution profile of batches TF-6, TF-7, TF-8, TF-9 and TF-10 formulations with pure drug.

Figure 8: Skin irritation photographs of SF-3 andTF-8 batch

DESCRIPTION OF THE INVENTION

The present invention is all about Proniosomal gel of Celecoxib.

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 Proniosomal gel of Celecoxib.

Another embodiment of the present invention provides Proniosomal gel of Celecoxib comprising:

i. Celecoxib,
ii. Lecithin,
iii. Cholesterol,
iv. Surfactant,
v. Polyacrylic acid

wherin ratio of Surfactant: Cholesterol is from 5:5 to 9:1.

As per another embodiment the active ingredient used is Celecoxib which is a nonsteroidal anti-inflammatory drug (NSAID) able to selectively inhibit COX-2 activity and exhibits antiinflammatory, analgesic and antipyretic activities.

As per another embodiment the concentration of Celecoxib is in the range of 50 to 150 mg.

As per another embodiment the Surfactant may include span 60, span 40, tween 20, tween80.

As per another embodiment the ratio of Surfactant: Cholesterol is selected from 5:5, 6:4, 7:3, 8:2 and 9:1.

As per another embodiment the concentration of Cholesterol is in the range of 10 to 600 mg.

As per another embodiment the concentration of Lecithin is in the range of 10 to 200 mg.

As per another embodiment the concentration of Polyacrylic acid is in the range of 0.1 to 10% w/v.

As per another embodiment, the present invention provides a process of preparing Proniosomal gel of Celecoxib by coacervation phase separation method comprising steps of:

1. Dissolving Celecoxib, Cholesterol, Lecithin and Surfactant in solvent and mixing it on warm water bath at 50 to 60°c to form a solution,
2. Adding few drops of pH 6.8 phosphate buffer into the solution to form a liquid gel,
3. Warming of liquid gel at 50 to 60°c and cooling down upto room temperature,
4. Incorporating the liquid gel of step 3 into required amount of polyacrylic acid and mixing well to obtain Proniosomal gel.

As per another embodiment, the present invention provides Proniosomal gel of Celecoxib for treating Osteoarthritis, rheumatoid arthritis, juvenile rheumatoid arthritis, ankylosing spondylitis, acute pain and primary dysmenorrhea.

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: Composition and process of Preparing Proniosomal gel of Celecoxib

Table 1 – Composition of Proniosomal gel of Celecoxib

Code	**Drug**	**Ratio S:C**	**Surfactant (S) (mg)**	**Cholesterol (C) (mg)**	**Lecithin (mg)**	**Carbopol**
SF 1	100	9:1	900	100	100	0.75%w/v Carbopol
SF 2	100	8:2	800	200	100	

SF 3	100	7:3	700	300	100	
SF 4	100	6:4	600	400	100	
SF 5	100	5:5	500	500	100	
SF 6	100	9:1	900	100	100	
SF 7	100	8:2	800	200	100	
SF 8	100	7:3	700	300	100	
SF 9	100	6:4	600	400	100	
SF 10	100	5:5	500	500	100	
TF 1	100	9:1	900	100	100	
TF 2	100	8:2	800	200	100	
TF 3	100	7:3	700	300	100	
TF4	100	6:4	600	400	100	
TF 5	100	5:5	500	500	100	
TF 6	100	9:1	900	100	100	
TF 7	100	8:2	800	200	100	
TF 8	100	7:3	700	300	100	
TF 9	100	6:4	600	400	100	
TF 10	100	5:5	500	500	100	

SF1 to SF5 comprises of span 60 as surfactant. SF6 to SF10 comprises of span 40 as surfactant. TF1 to TF5 comprises of tween 20 as surfactant. TF6 to TF10 comprises of tween 80 as surfactant. Celecoxib proniosomal gels were prepared by coacervation phase separation method. Precisely weighed amounts of surfactant, cholesterol, lecithin and Celecoxib were taken in a clean and dry wide mouthed glass vial of 5.0 ml capacity and methanol (2.5 ml) was added to it. All the ingredients were mixed well with a glass rod; the open end of the glass vial was covered with a lid to prevent the loss of solvent from it and warmed-over water bath at 50-600C for about 5 min until the drug is dissolved completely in surfactant mixture. 3 to 5 drops of pH 6.8 phosphate buffer was added**.** The mixture was allowed to cool to room temperature until the dispersion was converted to proniosomes. Preliminary composition of these formulations is referred as

SF1, SF2, SF3, SF4, SF5, SF6, SF7, SF8, SF9, SF10, TF1, TF2, TF3, TF4, TF5, TF6, TF7, TF8, TF9 and TF10. These proniosomal gels were incorporated into 0.75% w/v carbopol and the mixture was converted into proniosomal gels.

Example 2: Evaluation Of Proniosomal gel of Celecoxib

Physical appearance and pH determination: The physical appearance and homogeneity of the prepared gels were tested by visual observations after the gels have been set in the container and they were tested for their appearance and presence of any aggregates. The pH of various gel formulations was determined by using digital pH meter. 1 gm of gel was dissolved in 100 ml distilled water and stored for 2 hr. The measurement of pH of each formulation was done in triplicate and average values were calculated.

Celecoxib proniosomal gels prepared with span 60 have milky white gel whereas with span 40, tween 20, tween 80 produces translucent milky white gel. The pH of the all the proniosomal gels were in the range of 7.4 to 7.6.

Table 2- Physical appearance and pH of various compositions of proniosomal gel

Code	**Appearance**	**pH**
SF-1	Milky white gel	7.4
SF-2	Milky white gel	7.4
SF-3	Milky white gel	7.3
SF-4	Milky white gel	7.3
SF-5	Milky white gel	7.3
SF-6	Translucent milky white gel	7.5
SF-7	Translucent milky white gel	7.5
SF-8	Translucent milky white gel	7.5
SF-9	Translucent milky white gel	7.5
SF-10	Translucent milky white gel	7.5

TF-1	Translucent milky white gel	7.5
TF-2	Translucent milky white gel	7.5
TF-3	Translucent milky white gel	7.5
TF-4	Translucent milky white gel	7.5
TF-5	Translucent milky white gel	7.5
TF-6	Translucent milky white gel	7.5
TF-7	Translucent milky white gel	7.5
TF-8	Translucent milky white gel	7.5
TF-9	Translucent milky white gel	7.5
TF-10	Translucent milky white gel	7.5

Entrapment efficiency: Separation of unentrapped drug from the proniosomal gel was done by exhaustive dialysis method. The measured quantity of proniosomal gel i.e.,1 gm was taken into a dialysis tube to which osmosis cellulose membrane was securely attached to one side, the dialysis tube was suspended in 200 ml saline buffer pH 6.8, which was stirred on a magnetic stirrer. The unentrapped drug was separated from the proniosomal gel into the medium through osmosis cellulose membrane. After 6 hrs. of exhaustive dialysis, optical density values were noted and the estimation of the entrapped drug was carried out by UV spectrophotometric method. Calculatation of entrapment efficiency was done by using following equation.

$$\text{Entrapment effeciency} = \frac{\text{Amount of drug entrapped}}{\text{Total amount of drug}} \times 100$$

Proniosomal gels prepared with span 60 shows higher entrapment efficiency then the span 40 due to the longer saturated alkyl chain compared to that of span 40. As the concentration of cholesterol increases the entrapment efficiency increases. Longer size may also contribute the highest EE. Tween 20 has longer alkyl chain compared to tween 80. Hence, tween 20 shows higher entrapment efficiency than tween 80.

Table 3- Entrapment efficiency of various compositions of proniosomal gel

S. No	Formulation code	Entrapment efficiency%±SD
1	SF-1	93.20 ± 0.51
2	SF-2	94.20 ± 0.43
3	SF-3	96.01 ± 0.45
4	SF-4	92.70 ± 0.32
5	SF-5	90.05 ± 0.34
6	SF-6	90.10 ± 0.41
7	SF-7	89.30 ± 0.46
8	SF-8	87.11 ± 0.45
9	SF-9	84.15 ± 0.35
10	SF-10	84.55 ± 0.37
11	TF-1	95.12±0.21
12	TF-2	96.35 ± 0.44
13	TF-3	97.01 ± 0.22
14	TF-4	94.20 ± 0.23
15	TF-5	93.22 ± 0.11
16	TF-6	91.16±0.30
17	TF-7	93.42 ± 0.24
18	TF-8	92.01 ± 0.12
19	TF-9	89.02 ± 0.13
20	TF-10	88.32 ± 0.31

*Average of three determinations

Drug content: Proniosomal gel equivalent to 10 mg of drug were taken into a standard 25 ml volumetric flask. They were lysed with 25 ml of methanol by shaking for 15 min. Then 1 ml of this solution was diluted to 10 ml with phosphate buffer pH 6.8. Aliquots were withdrawn and the absorbance was measured at 253 nm and the drug content was calculated from the calibration curve.

The low standard deviation (SD) and low coefficient of variation (CV) i.e., <2 indicates drug distribution was uniform in all the preparations.

Table 4- Drug content of of various compositions of proniosomal gel

Formulation code	Amount of drug incorporated(mg)	Amount of drug recovered(mg)	% Drug content ±* SD
SF-1	10	9.53	95.3±0.22
SF-2	10	9.65	96.5±0.23
SF-3	10	9.90	99.0±0.32
SF-4	10	9.42	94.2±0.12

SF-5	10	9.62	96.2±0.22
SF-6	10	9.51	95.1±0.22
SF-7	10	9.68	96.8±0.42
SF-8	10	9.78	97.8±0.23
SF-9	10	9.62	96.2±0.32
SF-10	10	9.64	96.4±0.36
TF-1	10	9.23	92.3±0.21
TF-2	10	9.56	95.6±0.45
TF-3	10	9.15	91.5±0.23
TF-4	10	9.61	96.1±0.45
TF-5	10	9.29	92.9±0.44
TF-6	10	9.09	90.9±0.50
TF-7	10	9.04	90.4±0.45
TF-8	10	9.83	98.3±0.55
TF-9	10	9.78	97.8 ±0.55
TF-10	10	9.6	96.2 ±0.53

Particle size analysis: Particle size analysis was carried out using an optical microscope (compound microscope) with a calibrated eyepiece micrometer. From each batch about 200 proniosomes were measured for the individual diameter then average was calculated. The result suggests that proniosomes prepared were of uniform size and spherical in shape. The microphotographs of all proniosomes from proniosomal gel formulations reveal that the niosomes were spherical in their shape.

Table 5- Particle size distribution and average particle size of SF-1, SF-5 and SF-6 Celecoxib formulations

Size range(μ)	No of particles	Size range(μ)	No of particles	Size range(μ)	No of particles
0-4	42	0-4	54	0-4	48
5-8	67	5-8	69	5-8	81
9-12	53	9-12	51	9-12	44
13-16	38	13-16	26	13-16	27
Average particle size: 4.91μ		Average particle size: 4.43μ		Average particle size: 4.79μ	

Table 6- Particle size distribution and average particle size of SF- 10, TF-1 and TF-5 Celecoxib formulations

Size range(µ)	No of particles	Size range(µ)	No of particles	Size range(µ)	No of particles
0-4	43	0-4	43	0-4	49
5-8	83	5-8	79	5-8	76
9-12	48	9-12	46	9-12	44
13-16	26	13-16	32	13-16	31
Average particle size: 4.82 µ		Average particle size: 4.65 µ		Average particle size: 4.29 µ	

Table 7-Particle size distribution and average particle size of TF-6 and TF-10 Celecoxib formulations.

Size range(µ)	No of particles	Size range(µ)	No of particles	Size range(µ)	No of particles
0-4	43	0-4	43	0-4	49
5-8	83	5-8	79	5-8	76
9-12	48	9-12	46	9-12	44
13-16	26	13-16	32	13-16	31
Average particle size: 4.82 µ		Average particle size: 4.65 µ		Average particle size: 4.29 µ	

Table 8-Particle size distribution and average particle size of TF-6 and TF-10 Celecoxib formulations.

Size range(µ)	No of particles	Size range(µ)	No of particles
0-4	49	0-4	48
5-8	76	5-8	79
9-12	47	9-12	47
13-16	28	13-16	26
Average particle size: 4.83µ		Average particle size: 4.67µ	

Zeta potential analysis: The zeta potential was analyzed for proniosomalgel by Malvern Zetasizer atManipal university, Manipal. The zeta potential value for the optimized proniosomal gel SF-3 and TF-8 was found to be -78.3mVand -73.0M v respectively. A value of ±25 mV (positive or negative) was taken as the arbitrary value that separates low-charged surfaces from highly-charged surfaces. The zeta size distribution report SF-3 and TF-8 was found to be 1442d.nm and 3001d.nm respectively. All the proniosome formulations were negatively charged, which was due to the negative charge present on the lecithin. The zeta potential values were high in all the formulations. The high zeta potential increases the repulsion between the particles and thus prevents their aggregation and flocculation. So, it electrically stabilizes the system.

In vitro permeation studies: The release of celecoxib from proniosomal gel formulations were determined using membrane diffusion technique. The proniosomal gel equivalent to 10 mg of celecoxib was applied on the previously soaked osmosis cellulose membrane that was attached at one end of glass tube, which acts as a donor compartment. The glass tube was placed in a beaker containing 200 ml of phosphate buffer pH 6.8, which acts as receptor compartment. The whole assembly was fixed in such a way that the lower end of the tube containing proniosomal gel was just touched (1-2 mm deep) the surface of diffusion medium. The temperature of receptor medium maintained at 37 ± 50C and the medium was agitated at 100 rpm speed using magnetic stirrer. Aliquot of 1 ml sample were withdrawn periodically and after each withdrawn same volume of medium was replaced. The collected samples were analyzed at 253 nm in double beam UV-VIS spectrophotometer using phosphate buffer pH 6.8 as blank. The in vitro drug release and model fitting data was computed by using dissolution software PCP Disso V.3.

The cumulative percentage drug release of celecoxib proniosomal gel formulation show the drug release of about 20 to 40 % after 6h,its mainly due to initial bursting of improper proniosomes in formulations and at the start of 12h the release was found to be steady because stable proniosomes

retains the drug release and the release was extended up to 24h with sustained action. The in vitro drug release data obtained from the formulations were model fitted to check the mechanism of drug release using PCP DISSO V.3 software. The exponential 'n' values were found to be greater than 0.5 and less than 1.00 suggesting that the drug was released by non Fickian (anomalous) release mechanism i.e., the drug was released by erosion followed by diffusion controlled.

Table 9-Cumulative percentage drug released vs time for SF-1 to SF-5

Time in h	Cumulative percent drug released ±* SD					
	Pure drug	SF-1	SF-2	SF-3	SF-4	SF-5
0.5	4.48±0.21	3.35±0.11	3.91±0.12	3.91±0.20	5.27±0.15	5.27±0.22
1	5.83±0.16	5.89±0.19	4.56±0.21	6.48±0.19	7.67±0.29	7.56±0.19
1.5	7.35±0.15	7.75±0.20	4.89±0.18	7.47±0.22	9.40±0.19	8.60±0.28
2	11.67±0.20	9.92±0.15	5.34±0.17	8.49±0.18	10.87±0.20	10.02±0.11
2.5	15.12±0.30	11.84±0.22	5.92±0.22	10.34±0.19	12.02±0.30	12.16±0.21
3	20.43±0.22	13.61±0.14	6.39±0.25	11.36±0.23	13.22±0.25	14.39±0.19
3.5	29.35±0.14	16.57±0.21	7.11±0.19	12.52±0.21	15.13±0.18	15.68±0.25
4	40.94±0.11	20.55±0.23	8.64±0.17	14.51±0.18	16.66±0.14	17.12±0.27
4.5	49.20±0.19	21.76±0.21	9.43±0.23	17.92±0.17	18.12±0.22	18.83±0.31
5	57.11±0.22	23.56±0.24	10.71±0.34	19.44±0.13	20.52±0.21	20.48±0.18
5.5	61.24±0.35	26.41±0.18	12.03±0.31	20.55±0.20	23.57±0.28	21.94±0.14
6	66.81±0.24	29.02±0.11	13.95±0.25	21.79±0.36	26.95±0.31	24.79±0.23
6.5	73.77±0.21	30.58±0.10	18.21±0.20	24.18±0.18	31.60±0.17	27.07±0.27
7	81.18±0.19	33.07±0.35	22.09±0.11	28.23±0.22	34.84±0.21	30.09±0.14
7.5	91.29±0.20	36.63±0.21	24.21±0.18	32.43±0.21	39.76±0.22	32.43±0.19
8	98.59±0.22	43.37±0.22	25.83±0.15	37.25±0.17	44.98±0.28	37.30±0.35
9	-	48.57±0.19	31.43±0.17	43.15±0.16	50.15±0.30	41.35±0.19
10	-	51.69±0.15	39.74±0.20	47.69±0.12	54.94±0.27	44.97±0.22
11	-	55.67±0.20	47.84±0.31	51.37±0.33	60.44±0.15	50.50±0.18
12	-	58.40±0.22	52.32±0.35	57.62±0.15	64.98±0.19	56.91±0.34
14	-	62.08±0.19	56.03±0.38	62.74±0.28	67.84±0.27	61.29±0.28

16	-	66.29±0.18	60.17±0.25	68.58±0.32	71.18±0.31	64.89±0.26
18	-	71.85±0.21	67.11±0.21	73.80±0.17	75.36±0.24	69.01±0.11
20	-	77.13±0.22	72.14±0.19	79.96±0.11	78.38±0.22	73.68±0.26
24	-	80.75±0.25	83.51±0.20	86.19±0.15	82.23±0.18	80.61±0.33

*Average of three determinations.

Table 10-Cumulative percentage drug released vs time for SF-6 to SF-10

Time inh	Cumulative percent drug released ±* SD					
	Pure drug	SF-6	SF-7	SF-8	SF-9	SF-10
0.5	4.48±0.11	3.69±0.20	8.09±0.12	4.93±0.19	4.36±0.16	3.12±0.10
1	5.83±0.15	5.23±0.23	10.07±0.18	6.98±0.22	5.82±0.34	4.41±0.19
1.5	7.35±0.16	6.16±0.22	11.46±0.15	8.33±0.21	7.80±0.11	5.97±0.20
2	11.64±0.20	7.34±0.19	14.02±0.19	9.96±0.28	9.18±0.21	7.05±0.25
2.5	15.12±0.20	8.47±0.17	15.89±0.23	11.20±0.26	11.96±0.28	8.27±0.13
3	20.43±0.19	9.17±0.22	18.72±0.28	12.71±0.31	13.51±0.16	8.97±0.18
3.5	29.35±0.34	10.46±0.24	20.31±0.22	14.15±0.18	15.22±0.16	9.58±0.24
4	40.94±0.18	11.69±0.18	23.97±0.19	16.09±0.31	17.11±0.21	10.42±0.27
4.5	49.20±0.24	14.19±0.26	26.53±0.11	17.42±0.28	19.16±0.31	11.52±0.11
5	57.11±0.20	16.91±0.31	28.60±0.18	19.34±0.19	20.95±0.18	13.88±0.23
5.5	61.24±0.15	21.65±0.11	30.50±0.21	21.67±0.16	24.03±0.22	17.81±0.34
6	66.81±0.31	24.11±0.19	33.23±0.29	23.85±0.30	26.77±0.33	22.59±0.22
6.5	73.77±0.16	27.56±0.21	35.81±0.31	28.02±0.28	31.40±0.24	26.89±0.28
7	81.18±0.15	30.90±0.28	39.37±0.11	31.90±0.27	36.33±0.19	30.35±0.16
7.5	91.29±0.19	34.36±0.22	42.24±0.19	34.68±0.11	42.35±0.11	35.61±0.18
8	98.59±0.22	38.04±0.19	46.21±0.12	38.89±0.16	46.11±0.24	39.50±0.22
9	-	41.84±0.11	51.31±0.16	43.25±0.25	49.88±0.28	44.42±0.28
10	-	46.88±0.36	55.91±0.28	48.88±0.19	56.11±0.16	50.30±0.34

11	-	51.65±0.25	60.88±0.31	53.48±0.22	60.87±0.31	54.69±0.16
12	-	56.24±0.26	64.64±0.28	59.12±0.19	64.97±0.18	61.46±0.25
14	-	62.54±0.31	70.52±0.11	64.26±0.27	68.16±0.16	66.22±0.22
16	-	67.25±0.18	75.13±0.19	70.92±0.16	71.95±0.21	69.96±0.21
18	-	72.98±0.10	79.50±0.25	77.57±0.11	75.93±0.20	73.67±0.26
20	-	78.32±0.19	83.63±0.34	84.76±0.10	81.12±0.16	80.14±0.28
24	-	85.72±0.18	88.07±0.22	90.15±0.22	87.46±0.18	86.36±0.16

*Average of three determinations.

Table 11-Cumulative percentage drug released vs time for TF-1 to TF-5

Time inh	Cumulative percent drug released ±* SD					
	Pure drug	TF-1	TF-2	TF-3	TF-4	TF-5
0.5	4.48±0.16	3.69±0.19	2.56±0.21	2.45±0.11	4.25±0.31	2.56±0.19
1	5.83±0.22	4.55±0.10	4.04±0.16	3.47±0.20	5.14±0.26	4.15±0.12
1.5	7.35±0.24	5.44±0.23	5.25±0.20	5.33±0.26	6.85±0.22	5.37±0.22
2	11.64±0.11	6.37±0.18	6.18±0.15	6.71±0.24	8.75±0.19	6.30±0.28
2.5	15.12±0.19	8.01±0.31	7.81±0.19	9.50±0.28	11.30±0.25	7.94±0.31
3	20.43±0.21	9.72±0.17	9.63±0.24	11.51±0.31	13.49±0.19	9.65±0.14
3.5	29.35±0.31	10.82±0.19	11.96±0.31	13.83±0.16	16.34±0.16	10.75±0.16
4	40.94±0.29	12.74±0.22	13.84±0.28	16.58±0.18	18.40±0.25	12.67±0.25
4.5	49.20±0.28	14.29±0.34	16.00±0.22	18.30±0.20	21.76±0.29	14.21±0.24
5	57.11±0.16	17.69±0.18	18.58±0.19	21.99±0.24	25.60±0.19	17.61±0.28
5.5	61.24±0.19	20.44±0.15	21.15±0.14	25.04±0.31	29.02±0.18	20.36±0.12
6	66.81±0.31	24.98±0.16	24.93±0.31	29.44±0.19	32.66±0.31	24.91±0.16
6.5	73.77±0.18	29.37±0.15	27.96±0.20	34.12±0.22	36.89±0.28	29.30±0.11
7	81.18±0.24	35.51±0.11	30.97±0.22	36.95±0.31	40.13±0.19	35.44±0.19
7.5	91.29±0.32	39.53±0.21	34.99±0.18	40.75±0.19	43.35±0.24	39.46±0.10
8	98.59±0.19	44.59±0.23	39.14±0.19	46.13±0.24	46.88±0.15	44.51±0.22
9	-	49.02±0.31	43.10±0.31	50.13±0.28	51.40±0.22	48.95±0.19
10	-	53.26±0.28	46.62±0.15	54.92±0.22	56.64±0.19	53.18±0.15
11	-	59.98±0.24	53.05±0.24	61.09±0.31	60.23±0.25	59.91±0.32
12	-	63.22±0.33	58.03±0.19	64.54±0.23	64.59±0.18	63.14±0.19

14	-	67.63±0.19	62.60±0.25	68.62±0.29	68.49±0.16	67.56±0.25
16	-	71.70±0.16	70.22±0.22	73.12±0.13	72.02±0.28	71.63±0.21
18	-	76.08±0.22	75.41±0.18	77.40±0.22	76.30±0.22	75.45±0.26
20	-	79.66±0.24	80.06±0.31	81.54±0.19	79.54±0.34	78.65±0.31
24	-	82.83±0.26	83.45±0.15	85.75±0.28	82.71±0.19	81.67±0.16

*Average of three determinations.

Table 12-Cumulative percentage drug released vs time for TF-6 to TF-10

Time	Cumulative percent drug released ±* SD					
inh	Pure drug	TF-6	TF-7	TF-8	TF-9	TF-10
0.5	4.48±0.15	4.03±0.21	6.17±0.22	5.94±0.16	5.49±0.23	4.36±0.11
1	5.83±0.22	5.24±0.15	7.94±0.31	7.71±0.21	6.90±0.15	5.26±0.18
1.5	7.35±0.16	7.07±0.17	9.12±0.24	9.09±0.26	8.13±0.26	6.53±0.21
2	11.64±0.23	8.87±0.24	10.44±0.16	10.19±0.27	10.09±0.31	7.73±0.26
2.5	15.12±0.19	10.41±0.34	12.04±0.24	12.00±0.31	11.56±0.15	8.76±0.15
3	20.43±0.31	13.12±0.28	13.91±0.35	13.88±0.15	12.63±0.18	9.93±0.19
3.5	29.35±0.24	15.16±0.15	15.52±0.18	15.26±0.18	14.40±0.16	11.03±0.21
4	40.94±0.19	17.39±0.27	17.29±0.24	17.24±0.34	16.92±0.11	12.95±0.19
4.5	49.20±0.15	19.69±0.19	19.00±0.11	18.96±0.25	19.19±0.21	14.49±0.24
5	57.11±0.24	22.87±0.24	22.57±0.16	21.28±0.29	21.76±0.31	17.89±0.30
5.5	61.24±0.19	25.48±0.31	24.70±0.10	23.58±0.30	23.98±0.26	20.64±0.35
6	66.81±0.24	28.18±0.18	27.23±0.28	26.62±0.26	26.49±0.14	24.63±0.19
6.5	73.77±0.31	30.97±0.16	31.19±0.24	31.01±0.20	31.44±0.21	30.79±0.18
7	81.18±0.18	33.95±0.24	33.95±0.31	33.77±0.26	35.58±0.29	35.19±0.15
7.5	91.29±0.14	37.36±0.26	37.80±0.16	37.62±0.26	38.40±0.25	39.75±0.24
8	98.59±0.26	43.36±0.31	41.33±0.25	41.04±0.21	42.08±0.31	45.14±0.28
9	-	47.00±0.15	45.42±0.14	44.90±0.31	47.00±0.15	49.26±0.16
10	-	52.77±0.27	49.86±0.24	49.55±0.16	52.66±0.14	53.49±0.18
11	-	56.93±0.16	54.00±0.29	54.01±0.25	58.18±0.21	60.21±0.16
12	-	60.31±0.24	58.59±0.14	57.71±0.10	62.07±0.29	63.45±0.19
14	-	64.55±0.22	63.65±0.21	64.21±0.32	66.05±0.24	67.86±0.26
16	-	68.55±0.35	68.86±0.16	69.35±0.16	69.89±0.10	71.93±0.31

18	-	72.64±0.28	73.78±0.25	73.51±0.25	74.15±0.22	75.75±0.28
20	-	76.71±0.24	77.70±0.28	78.33±0.19	78.06±0.26	78.96±0.16
24	-	79.97±0.15	83.16±0.26	85.40±0.12	81.03±0.18	82.31±0.30

*Average of three determinations.

Example 3: Skin irritancy test

Skin irritancy test Irritancy test was carried out to determine possible localized reaction of the prepared gel on the skin since skin safety is of prior consideration for transdermal delivery systems. Albino Rabbits (1.4-1.5kg) males were used for testing of skin irritation. The animals were maintained on standard animal feed and had free access to water. The animals were kept under standard conditions. Hair was shaved from back of rabbits and area of $4cm^2$ was marked on both the sides. One side served as control white the other side was test. Prepared optimized proniosome gel was applied (140 mg/rabbits) on first day andthe development of erythema was monitored daily for 7 days. Extents of development of erythema were indicated on the basis of the following the site was observed for any sensitivity and reaction if any, was graded as 0, 1, 2, 3 for no reaction, slightly patchy erythema, slightly but conflict or moderate patchy erythema, severe erythema with or without edema respectively.

Irritation potential was calculated using the following equation:

$$\text{Resultant index} = \frac{\text{A X B}}{\text{Number of observation in days}}$$

Where A and B represent erythema value and corresponding day, respectively.

The selected proniosome gel formulation (SF-3 and TF-8) showed an irritation potential of 0.31 and 0.45, thus proving to be non-irritant as a value between 0 and 1 in an irritancy test indicates that the applied formulation is generally non-irritant to human skin. No obvious erythema, oedema or inflammation was observed on rabbits' skin after one week of application of the selected formulations (depicted in figure 8) indicating celecoxib proniosomal gel can be conveniently applied without any irritation.

We Claim,

1. A Proniosomal gel of Celecoxib comprising:
    i. Celecoxib,
    ii. Lecithin,
    iii. Cholesterol,
    iv. Surfactant,
    v. Polyacrylic acid

wherin ratio of Surfactant: Cholesterol is from 5:5 to 9:1.

2. The Proniosomal gel of Celecoxib as claimed in claim 1 wherein, the concentration of Celecoxib is in the range of 50 to 150 mg.

3. The Proniosomal gel of Celecoxib as claimed in claim 1 wherein, the Surfactant is selected from span 60, span 40, tween 20, tween80.

4. The Proniosomal gel of Celecoxib as claimed in claim 1 wherein, the ratio of Surfactant: Cholesterol is selected from 5:5, 6:4, 7:3, 8:2 and 9:1.

5. The Proniosomal gel of Celecoxib as claimed in claim 1 wherein, the concentration of Cholesterol is in the range of 10 to 600 mg.

6. The Proniosomal gel of Celecoxib as claimed in claim 1 wherein, the concentration of Lecithin is in the range of 10 to 200 mg.

7. The Proniosomal gel of Celecoxib as claimed in claim 1 wherein, the concentration of Polyacrylic acid is in the range of 0.1 to 10% w/v.

Dated this 1st September 2021

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

ABSTRACT

PRONIOSOMAL GEL OF CELECOXIB

The present invention is related to Proniosomal gel of Celecoxib and its method of preparation. The said Proniosomal gel provides sustained release of the drug for over 24 hours therby enhancing biavailability of Celecoxib and is useful for treating Osteoarthritis.

FORM 9

THE PATENTS ACT, 1970

(39 OF 1970)

&

The Patents Rules, 2003

REQUEST FOR PUBLICATION

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

---

1. Name, address and Nationality of the applicant (s)	~~I~~/ We 1. DR. SRIKANTH 2. DR. SHUBHRAJIT MANTRY 3. DR. DIPANSU SAHU 4. MR. TEJAS J. PATEL 5. DR. SHRIRAM RAMESH PETHAKAR 6. MRS. JYOTI BALAJI ARSUDE hereby request for early publication of ~~my~~/our application for patent No. 202141039628 dated 2021/09/01 under section 11A(2) of the act.

Dated this 8th day of September 2021.

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