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Application Details

APPLICATION NUMBER	201821015784
APPLICATION TYPE	ORDINARY APPLICATION
DATE OF FILING	26/04/2018
APPLICANT NAME	1 . JOSHI SUMIT ASHOK 2 . JALALPURE SUNIL SATYAPPA 3 . PANCHAL CHANDRAWADAN VISHWAMBHAR 4 . KEMPWADE AMOLKUMAR ASHOK 5 . VENKATA SIVA NAGA MALLESWARA RAO PERAM 6 . PETHAKAR SHRIRAM RAMESH
TITLE OF INVENTION	NANOSTRUCTURED LIPID CARRIERS (NLCS) BASED TRANSDERMAL PATCHES OF COLCHICINE
FIELD OF INVENTION	CHEMICAL
E-MAIL (As Per Record)	vijay@patlex.in
ADDITIONAL-EMAIL (As Per Record)	sumit.ajoshi87@gmail.com
E-MAIL (UPDATED Online)	
PRIORITY DATE	

REQUEST FOR EXAMINATION DATE	14/10/2020
PUBLICATION DATE (U/S 11A)	22/06/2018
REPLY TO FER DATE	22/12/2020

Application Status

APPLICATION STATUS

Reply Filed. Application in amended examination[View Documents](#)

➔ Filed ➔ Published ➔ RQ Filed ➔ Under Examination ➔ Disposed

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. 25/2018
ISSUE NO. 25/2018

शुक्रवार
FRIDAY

दिनांक: 22/06/2018
DATE: 22/06/2018

पेटेंट कार्यालयका एक प्रकाशन
PUBLICATION OF THE PATENT OFFICE

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(19) INDIA

(22) Date of filing of Application :26/04/2018

(43) Publication Date : 22/06/2018

(54) Title of the invention : NANOSTRUCTURED LIPID CARRIERS (NLCS) BASED TRANSDERMAL PATCHES OF COLCHICINE

(51) International classification	:A61K31/353	(71)Name of Applicant :
(31) Priority Document No	:NA	1)JOSHI SUMIT ASHOK
(32) Priority Date	:NA	Address of Applicant :AT. POST. PATHARE, TALUKA
(33) Name of priority country	:NA	SINNAR, DIST. NASHIK-422 104, MAHARASHTRA, INDIA
(86) International Application No	:NA	Maharashtra India
Filing Date	:NA	2)JALALPURE SUNIL SATYAPPA
(87) International Publication No	:NA	3)PANCHAL CHANDRAWADAN VISHWAMBHAR
(61) Patent of Addition to Application Number	:NA	4)KEMPWADE AMOLKUMAR ASHOK
Filing Date	:NA	5)VENKATA SIVA NAGA MALLESWARA RAO PERAM
(62) Divisional to Application Number	:NA	6)PETHAKAR SHRIRAM RAMESH
Filing Date	:NA	(72)Name of Inventor :
		1)JOSHI SUMIT ASHOK
		2)JALALPURE SUNIL SATYAPPA
		3)PANCHAL CHANDRAWADAN VISHWAMBHAR
		4)KEMPWADE AMOLKUMAR ASHOK
		5)VENKATA SIVA NAGA MALLESWARA RAO PERAM
		6)PETHAKAR SHRIRAM RAMESH

(57) Abstract :

The present invention relates to Nanostructured Lipid Carriers (NLCS) based transdermal patches of Colchicine and a process for preparation thereof.

No. of Pages : 20 No. of Claims : 10

D. No. 19333

E-107/4533/2018

Date: 26th April, 2018

To,

The Controller of Patents & Designs,

Patent Office Branch, Mumbai,

S. M. Road, Antop Hill, Mumbai - 400037.



200231611

Subject: Filing of Indian complete patent application entitled, "Nanostructured Lipid Carriers (NLCs) based transdermal patches of Colchicine".

Dear Sir,

We intend to file complete patent application for an invention entitled; "Nanostructured Lipid Carriers (NLCs) based transdermal patches of Colchicine". Please find enclosed herewith the following documents for the same:

- Form 1
- Form 2
- Form 3
- Form 5
- Form 9
- Abstract
- Cash Rs 4500.

We request you to take these documents on record and acknowledge the receipt of the documents.

Thanking you.

Yours sincerely,

JOSHI Sumit Ashok

At. Post. Pathare,

Taluka Sinnar, Dist. Nashik, 422104,

Maharashtra, India.

I P O M U M B A I 2 6 - 0 4 - 2 0 1 8 1 6 : 3 5



FORM 9

THE PATENTS ACT, 1970

(39 OF 1970)

&

The Patents Rules, 2003

REQUEST FOR PUBLICATION

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

27506 रूपये मकान/वेध/मभा अंडर कर
CBR संख्या... 7.7.82 दि... 26.04.2018
के प्रकृत प्राप्त हुए।
सिकदिया

1. Name, address and
Nationality of the applicant (s)

I/ We

1. JOSHI Sumit Ashok;

2. JALALPURE Sunil Satyappa;

3. PANCHAL Chandrawadan Vishwambhar;

4. KEMPSWADE Amolkumar Ashok;

5. VENKATA Siva Naga Malleswara Rao
Peram;

6. PETHAKAR Shriram Ramesh

hereby request for early publication of
my/our application for patent No.

dated _____ under
section 11A(2) of the act.

Dated this ²⁶ day of April 2018.

Signature

(Mr. JOSHI Sumit Ashok)

At. Post. Pathare, Taluka
Sinnar, Dist. Nashik, 422104,
Maharashtra, India

I P O M U M B A I 2 6 - 0 4 - 2 0 1 8 1 6 : 3 5

2. To be signed by the applicant or his authorized registered patent agent.

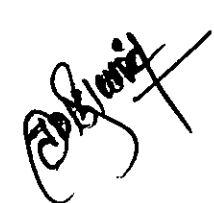
Name of the person who has signed

To,
The Controller of Patents,
The Patent Office,
At Mumbai.

E-S | 741 | 2018



200231614

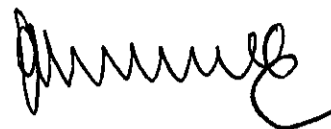
FORM 5 THE PATENTS ACT, 1970 (39 OF 1970) & The Patents Rules, 2003 DECLARATION AS TO INVENTORSHIP [See section 10 (6) and rule 13(6)]	
1. NAME OF THE APPLICANT (S)	1. JOSHI Sumit Ashok 2. JALALPURE Sunil Satyappa 3. PANCHAL Chandrawadan Vishwambhar 4. KEMPSWADE Amolkumar Ashok 5. VENKATA Siva Naga Malleswara Rao Peram 6. PETHAKAR Shriram Ramesh
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 JOSHI Sumit Ashok; JALALPURE Sunil Satyappa; PANCHAL Chandrawadan Vishwambhar; Dr. KEMPSWADE Amolkumar Ashok; VENKATA Siva Naga Malleswara Rao Peram and PETHAKAR Shriram Ramesh.	
2. INVENTORS	
<u>INVENTOR (1)</u>	
(a) NAME:	<u>JOSHI Sumit Ashok.</u>
(B) NATIONALITY:	Indian
(C) ADDRESS:	At. Post. Pathare, Taluka Sinnar, Dist. Nashik, 422104, Maharashtra, India. Dated this 26 th April 2018
	Signature: - 
	Name of the signatory: - <u>JOSHI Sumit Ashok.</u>
<u>INVENTOR (2)</u>	
(a) NAME:	<u>JALALPURE Sunil Satyappa.</u>
(B) NATIONALITY:	Indian
(C) ADDRESS:	KLEU's College of Pharmacy and Dr. Prabhakar Kore Basic Science Research Center, KLE University Nehru Nagar, Belagavi, 590010, Karnataka, India.

I P O M U M B A I 2 6 - 0 4 - 2 0 1 8 1 6 : 3 5

26-Apr-2018/193333/201821015784/Form 5

Dated this 26th April 2018

Signature: -



Name of the signatory: - JALALPURE Sunil Satyappa.

INVENTOR (3)

(a) NAME: PANCHAL Chandrawadan Vishwambhar.

(B) NATIONALITY: Indian

(C) ADDRESS: Maharashtra College of Pharmacy, Nilanga, 413521,
Maharashtra, India.

Dated this 26th April 2018

Signature: -



Name of the signatory: - PANCHAL Chandrawadan Vishwambhar

INVENTOR (4)

(a) NAME: KEMPSWADE Amolkumar Ashok.

(B) NATIONALITY: Indian

(C) ADDRESS: Dept. of Pharmaceutics, KLE's College of Pharmacy,
Nipani, 591237, Karnataka, India.

Dated this 26th April 2018

Signature: -



Name of the signatory: - KEMPSWADE Amolkumar Ashok

INVENTOR (5)

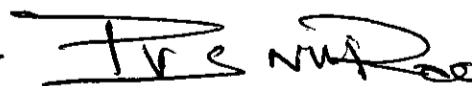
(a) NAME: VENKATA Siva Naga Malleswara Rao Peram.

(B) NATIONALITY: Indian

(C) ADDRESS: KLEU's College of Pharmacy and Dr. Prabhakar Kore Basic Science
Research Center, KLE University Nehru Nagar, Belagavi, 590010,
Karnataka, India.

Dated this 26th April 2018

Signature: -



Name of the signatory: - VENKATA Siva Naga Malleswara Rao Peram

INVENTOR (6)

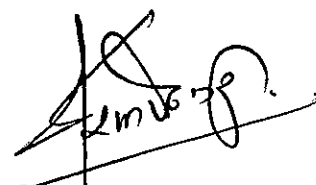
(a) NAME: PETHAKAR Shriram Ramesh.

(B) NATIONALITY: Indian

(C) ADDRESS: Latur College of Pharmacy, Hasegaon, Taluka Ausa,
Dist. Latur, 590010, Maharashtra, India.

Dated this 26th April 2018

Signature: -



Name of the signatory: - PETHAKAR Shriram Ramesh

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)

¶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 2018.

Signature of the additional inventor(s) : -

Name: -

To, The Controller of Patent,
The Patent Office, at... **Mumbai**...

23/5095/2018



200231613

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),

#We

1. **JOSHI Sumit Ashok**

At. Post. Pathare, Taluka Sinnar, Dist. Nashik, 422104,
Maharashtra, India.

2. **JALALPURE Sunil Satyappa**

KLEU's College of Pharmacy and Dr. Prabhakar Kore Basic
Science Research Center, KLE University Nehru Nagar,
Belagavi, 590010, Karnataka, India.

3. **PANCHAL Chandrawadan Vishwambhar**

Maharashtra College of Pharmacy, Nilanga, 413521,
Maharashtra, India.

4. **Dr. KEMPSWADE Amolkumar Ashok**

Dept. of Pharmaceutics, KLE's College of Pharmacy, Nipani,
591237, Karnataka, India.

5. **VENKATA Siva Naga Malleswara Rao Peram**

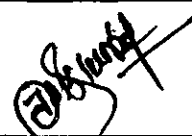
KLEU's College of Pharmacy and Dr. Prabhakar Kore Basic
Science Research Center, KLE University Nehru Nagar,
Belagavi, 590010, Karnataka, India.

6. **PETHAKAR Shriram Ramesh**

Latur College of Pharmacy, Hasegaon, Taluka Ausa, Dist.
Latur, 590010, Maharashtra, India.

hereby declare,

I P O M U M B A I 2 6 - 0 4 - 2 0 1 8 1 6 : 3 5

2. Name, address and nationality of the joint applicant		(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:			
Name of the country	Date of application	Application No	Status of the application	Date of publication	Date of grant
N/A					
3. Name and address of the assignee		(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 26 th day of April 2018			
4. To be signed by the applicant or his authorized patent agent		Signature 			
5. Name of the natural person who has signed		<u>JOSHI Sumit Ashok</u> At. Post. Pathare, Taluka Sinnar, Dist. Nashik, 422104, Maharashtra, India.			
		To, The Controller of Patents, The Patent Office, at...Mumbai...			
Note: - Strike out whichever is not applicable					

CE-29 876/2508

FORM 2

**THE PATENT ACT 1970
(39 of 1970)
&
The Patents Rules, 2003
COMPLETE SPECIFICATION
(See section 10 and rule13)**



1. TITLE OF THE INVENTION:

Nanostructured Lipid Carriers (NLCs) based transdermal patches of Colchicine.

2. APPLICANT (S)

(a) NAME:

1. JOSHI Sumit Ashok
2. JALALPURE Sunil Satyappa
3. PANCHAL Chandrawadan Vishwambhar
4. KEMPSWADE Amolkumar Ashok
5. VENKATA Siva Naga Malleswara Rao Peram
6. PETHAKAR Shriram Ramesh

(b) NATIONALITY: Indian

(c) ADDRESS:

1. At. Post. Pathare, Taluka Sinnar, Dist. Nashik, 422104, Maharashtra, India.
2. KLE College of Pharmacy and Dr. Prabhakar Kore Basic Science Research Center, KLE AHER, Nehru Nagar, Belagavi, 590010, Karnataka, India.
3. Maharashtra College of Pharmacy, Nilanga, 413521, Maharashtra, India.
4. Dept. of Pharmaceutics, KLES's College of Pharmacy, Nipani, 591237, Karnataka, India.
5. KLE College of Pharmacy and Dr. Prabhakar Kore Basic Science Research Center, KLE AHER, Nehru Nagar, Belagavi, 590010, Karnataka, India.

6. Latur College of Pharmacy, Hasegaon, Taluka Ausa,
Dist. Latur, 413531, Maharashtra, India.

3. PREAMBLE TO THE DESCRIPTION

The present invention relates to Nanostructured Lipid Carriers (NLCs) based transdermal patches of Colchicine and a process for preparation thereof.

4. DESCRIPTION (Description shall start from the next page.)

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

Technical field of the invention:

The present invention relates to Nanostructured Lipid Carriers (NLCs) based transdermal patches of Colchicine and a process for preparation thereof.

Background of the invention:

Gout is oldest rheumatological disease identified by Egyptians in 2640 BC. It was defined as "arthritis of rich" by Hippocrates as it was associated with life style, certain diet, and excessive alcohol consumption. It is most common form of arthritis (inflammatory), occurs due to crystal deposition of monosodium urate in soft tissues as well as surrounding the joints. It is a most painful condition characterized by swelling, pain, redness and heat in the joints. Most common location of gout attack is metatarsophalangeal joint. As per the reported statistics, pervasiveness of gout in New-zealand is highest (6.1%) in comparison with United States of America (3.9%) and United Kingdom (ranges from 1.4 to 2.5%). It was observed that, almost 16% of affected population is young generation having age group of around 30 years, nevertheless, since last 20 years; the occurrence has been substantially increased. This denotes an alarming condition and demands a special attention. Presently in the line of treatment for the management of gout, NSAID's (non-steroidal anti-inflammatory drugs), uricosuric compounds, corticosteroids are preferred choice.

However, in case of patients with renal disease, duodenal ulcers and cardiac diseases, NSAID's are contraindicated. Even, uricosuric drug (allopurinol) cannot be used in the initial stages, unless the acute attack has been settled (2 to 3 weeks), as it may aggravate the condition. Colchicine is a plant (*Colchicum autumnale*) derived alkaloid which is found to be most potent with short onset of action for the treatment of gout. Colchicine acts by inhibiting delocalization (migration) of neutrophils and leucocytes as well as through obstruction of formation of microtubules. However, a recent study showed that colchicine can also be used for the suppression of neutrophil superoxide production alone at doses 100 times lower than that necessary to prevent neutrophil infiltration. These findings have provided a rationale for

using low-dose colchicine for the treatment of gout. Side effects such as GI disturbance, diarrhea, nausea, and vomiting are observed in almost 80% of patients which is indicative of high risk/benefit ratio at a dosage of up to 1mg/2 hrs for more than a week. Longer duration of treatment with colchicine results in accumulation in body resulting in bone marrow suppression and neuromyopathy in patients with renal disease. Various studies were performed to surpass the difficulties arising due to administration of colchicine by oral route. Many studies have been undertaken by varying route of administration such as topical and transdermal formulations of colchicine. The reported studies have certain limitations like complexity of preparation and stability issues of formulations. Hence, there is need to develop a formulation of such potent drug which will improve the bioavailability and improve the benefit / risk ratio of colchicine for the management of gout.

In recent years, nanosized drug delivery systems have been studied for improving the bioavailability. These systems can be divided into separate groups like polymeric nanoparticles and lipid nanoparticles. The lipid nanoparticles provide less toxicological risk compared to polymeric nanoparticles owing to the natural and biological origins of the materials. Solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) are two major types of Lipid-based nanoparticles.

A research paper of the inventors of the invention Journal of Drug Delivery Science and Technology, Volume 41, October 2017, Pages 444-453 titled, "Fabrication and in-vivo evaluation of lipid nanocarriers based transdermal patch of colchicine" evaluated the use of SLNs for preparation of a transdermal patch of colchicine.

In the next generation of the lipid nanoparticles, NLCs are modified SLNs in which lipodic phase is contained both solid (fat) and liquid (oil) lipids at ambient temperature. In fact, NLCs are modified generations of SLNs that presenting a mixture of solid and liquid phase (oil) forming a formless matrix, which improves the stability and capacity loading. NLCs show contrasts with SLNs: more loading capacity for some drugs, some less water in the

dispersion, prevent or minimize the drug expulsion during storage, but not reported significant difference between the biotoxicity of SLNs and NLCs.

The inventors of the present invention have prepared Nanostructured Lipid Carriers (NLCs) based transdermal patches of Colchicine.

Summary of the invention:

The present invention relates to Nanostructured Lipid Carriers (NLCs) based transdermal patches of Colchicine and a process for preparation thereof.

In an embodiment, the present invention relates to a pharmaceutical composition comprising colchicine in the form of transdermal patches, based on Nanostructured Lipid Carriers (NLCs).

In an aspect of the embodiment, the composition comprises pharmaceutically acceptable inert excipients. In a specific aspect of the embodiment, the pharmaceutically acceptable inert excipients comprise polymers, plasticizers and solvents.

In another aspect of the embodiment, the lipid carriers are in the form of solid lipids. In a specific aspect of the embodiment, the solid lipid is selected from the group consisting of tristearin, stearic acid, cetyl palmitate, cholesterol, glyceryl palmitostearate, glyceryl dibehenate, microcrystalline triglyceride, Bis-Diglyceryl Polyacyladipate, glyceryl monostearate, Glyceryl Stearate Citrate and cetyl alcohol.

In another aspect of the embodiment, the lipid carriers are in the form of liquid lipids. In a specific aspect of the embodiment, the liquid lipid is selected from the group consisting of medium chain glycerides, castor oil, capric triglyceride, paraffin oil, 2-octyl dodecanol, oleic acid, squalene, isopropyl myristate, vitamin E and diethylene glycol monoethyl ether.

In yet another aspect of the embodiment, the lipid is in the form of combination of solid lipids and liquid lipids.

In another embodiment, the present invention relates to Nanostructured Lipid Carriers (NLCs) based transdermal patches of Colchicine for the treatment of gout.

In a subsequent embodiment, the present invention relates to process for preparing pharmaceutical composition comprising colchicine in the form of transdermal patches, based on Nanostructured Lipid Carriers (NLCs), the process comprising the steps of:

- a. Preparing the Nanostructured Lipid Carriers comprising solid and liquid lipids; and
- b. Preparing the transdermal patches using the Nanostructured Lipid Carriers prepared in step (a).

Detailed description of the invention:

The present invention relates to Nanostructured Lipid Carriers (NLCs) based transdermal patches of Colchicine and a process for preparation thereof.

The terms used in the specification are defined as follows.

The term "effective amount" or "therapeutically effective amount" refers to the amount of an active agent sufficient to induce a desired biological result. That result may be alleviation of the signs, symptoms, or causes of a disease, or any other desired alteration of a biological system. The term "therapeutically effective amount" is used herein to denote any amount of the formulation which causes improvement in a disease condition when applied to the affected areas repeatedly over a period of time. The amount will vary with the condition being treated, the stage of advancement of the condition, and the type and concentration of formulation applied. Appropriate amounts in any given instance will be readily apparent to those skilled in the art or capable of determination by routine experimentation.

As used herein, "treatment" or "treating," or "ameliorating" are used interchangeably. These terms refer to an approach for obtaining beneficial or desired results including but not limited to a therapeutic benefit and/or a prophylactic benefit. By therapeutic benefit is meant eradication or amelioration of the underlying disorder being treated. Also, a therapeutic benefit is achieved with the eradication or amelioration of one or more of the physiological symptoms associated with the underlying disorder such that an improvement is observed in the patient, notwithstanding that the patient may still be afflicted with the underlying disorder. For prophylactic benefit, the compositions may be administered to a patient at risk of developing a particular disease, or to a patient reporting one or more of the physiological symptoms of a disease, even though a diagnosis of this disease may not have been made. Treatment includes preventing the disease, that is, causing the clinical symptoms of the disease not to develop by administration of a protective composition prior to the induction of the disease; suppressing the disease, that is, causing the clinical symptoms of the disease not to develop by administration of a protective composition after the inductive event but prior to the clinical appearance or reappearance of the disease; inhibiting the disease, that is, arresting the development of clinical symptoms by administration of a protective composition after their initial appearance; preventing re-occurring of the disease and/or relieving the disease, that is, causing the regression of clinical symptoms by administration of a protective composition after their initial appearance.

A "subject," "individual," or "patient," is used interchangeably herein, which refers to a vertebrate, preferably a mammal, more preferably a human. Tissues, cells and their progeny of a biological entity obtained in vitro or cultured in vitro are also encompassed.

The use of the terms "a" and "an" and "the" and similar referents in the context of describing the elements (especially in the context of the following claims) are to be construed to cover both the singular and the plural, unless otherwise indicated herein or clearly contradicted by context. The terms

"comprising," "having," "including," and "containing" are to be construed as open-ended terms (i.e., meaning "including, but not limited to,") unless otherwise noted. Recitation of ranges of values herein are merely intended to serve as a shorthand method of referring individually to each separate value falling within the range, unless otherwise indicated herein, and each separate value is incorporated into the specification as if it were individually recited herein. All methods described herein can be performed in any suitable order unless otherwise indicated herein or otherwise clearly contradicted by context. The use of any and all examples, or exemplary language (e.g., "such as") provided herein, is intended merely to better illuminate the embodiments and does not pose a limitation on the scope of the claims unless otherwise stated. No language in the specification should be construed as indicating any non-claimed element as essential to the practice of the invention.

As used herein, "about" will be understood by persons of ordinary skill in the art and will vary to some extent depending upon the context in which it is used. If there are uses of the term in which are not clear to persons of ordinary skill in the art, given the context in which it is used, "about" will mean up to plus or minus 10% of the particular term.

The compositions comprise one or more pharmaceutically acceptable inert excipients. The term "pharmaceutically acceptable inert excipients", denotes any of the components of a pharmaceutical composition other than the active and which are approved by regulatory authorities or are generally 'regarded as safe' for human or animal use. A combination of excipients may also be used. The amount of excipient(s) employed will depend upon how much active agent is to be used. One excipient can perform more than one function.

A transdermal patch is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin and into the bloodstream. The main components to a transdermal patch are:

- Liner - Protects the patch during storage. The liner is removed prior to use.

- Adhesive - Serves to adhere the components of the patch together along with adhering the patch to the skin.
- Membrane - Controls the release of the drug from the reservoir and multi-layer patches.
- Backing - Protects the patch from the outer environment
- Permeation Enhancer - These are permeation promoters for drugs, which increases delivery of drug.
- Matrix Filler - It provides bulk to matrix as well as some of fillers acts as matrix stiffening agent.

In an embodiment, the present invention relates to a pharmaceutical composition comprising colchicine in the form of transdermal patches, based on Nanostructured Lipid Carriers (NLCs).

In an aspect of the embodiment, the composition comprises pharmaceutically acceptable inert excipients. In a specific aspect of the embodiment, the pharmaceutically acceptable inert excipients comprise polymers, plasticizers and solvents.

Polymers are the backbone of a transdermal drug delivery system. Systems for transdermal delivery are fabricated as multilayered polymeric laminates in which a drug reservoir or a drug-polymer matrix is sandwiched between two polymeric layers: an outer impervious backing layer that prevents the loss of drug through the backing surface and an inner polymeric layer that functions as an adhesive and/or rate-controlling membrane. The polymers used in the preparation of transdermal patch may include one or more of ethyl cellulose, hydroxypropyl methyl cellulose, eudragits, acrylates, soybean lecithin, vinyl polymers, silicone oil, polyisobutylene, 2-Ethylhexyl

acrylate, silicone elastomer, polyvinyl alcohol, polyvinyl pyrrolidine and the like. Preferably, ethyl cellulose and/or polyvinyl pyrrolidine are used.

Plasticizers are low molecular weight resins or liquids, which cause a reduction in polymer-polymer chain secondary bonding, forming secondary bonds with the polymer chains instead. The reasons for the use of plasticizers in transdermal drug delivery systems are the improvement of film forming properties and the appearance of the film, decreasing the glass transition temperature of the polymer, preventing film cracking, increasing film flexibility and obtaining desirable mechanical properties. One of the many advantages of plasticizers used in transdermal formulations is the controlling of the release rate of therapeutic compound which can be done by the selection of the plasticizer type and the optimization of its concentration in the formulation. The commonly used plasticizers in transdermal patches include phthalate esters, phosphate esters, fatty acid esters and glycol derivatives. Specific examples include Glycerine, Glycerine triacetate, Glyceryl tributyrate, Propylene glycol, Polyethylene glycol, Dibutyl phthalate, Diethyl phthalate, Dibutyl sebacate, Diethyl sebacate, Oleyl oleate, Sorbitol, Triethyl citrate, Tributyl citrate, Diethyl tartarate and the like. Preferably, triethyl citrate is used as a plasticizer in the transdermal patch. The plasticizers added to transdermal therapeutic systems are mostly used in the proportions between 5-20% of the total weight of the patch.

The solvents used in the transdermal patches include one or more of ethanol, chloroform, Octyldodecanol, isopropyl myristate, Oleyl alcohol, Polysorbate 80, Triacetin, Propylene glycol and the like.

The selection of excipients and the concentration thereof is based on the properties of the drug.

In another aspect of the embodiment, the lipid carriers are in the form of solid lipids. In a specific aspect of the embodiment, the solid lipid is selected from the group consisting of tristearin, stearic acid, cetyl palmitate, cholesterol, glyceryl palmitostearate, glyceryl dibehenate, microcrystalline

triglyceride, Bis-Diglyceryl Polyacyladipate, glyceryl monostearate, Glyceryl Stearate Citrate and cetyl alcohol. The commercially available solid lipids can be used for the preparation of the Nanostructured Lipid Carriers (NLCs).

In another aspect of the embodiment, the lipid carriers are in the form of liquid lipids. In a specific aspect of the embodiment, the liquid lipid is selected from the group consisting of medium chain glycerides, castor oil, capric triglyceride, paraffin oil, 2-octyl dodecanol, oleic acid, squalene, isopropyl myristate, vitamin E and diethylene glycol monoethyl ether. The commercially available liquid lipids can be used for the preparation of the Nanostructured Lipid Carriers (NLCs).

In yet another aspect of the embodiment, the lipid is in the form of combination of solid lipids and liquid lipids.

In another embodiment, the present invention relates to Nanostructured Lipid Carriers (NLCs) based transdermal patches of Colchicine for the treatment of gout. The colchicine used in such composition is therapeutically effective. The method for such treatment includes the administration of such a composition to the individual in need thereof.

In a subsequent embodiment, the present invention relates to process for preparing pharmaceutical composition comprising colchicine in the form of transdermal patches, based on Nanostructured Lipid Carriers (NLCs), the process comprising the steps of:

- a. Preparing the Nanostructured Lipid Carriers comprising solid and liquid lipids; and
- b. Preparing the transdermal patches using the Nanostructured Lipid Carriers prepared in step (a).

The Nanostructured Lipid Carriers (NLCs) according to the present invention can be prepared by any of the suitable methods like hot homogenization, cold homogenization or microemulsion method.

The transdermal patches according to the invention can be prepared by conventional methods based on the type of transdermal patch.

The foregoing examples are illustrative embodiments and are merely exemplary. A person skilled in the art may make variations and modifications without deviating from the spirit and scope of the invention. All such modifications and variations are intended to be included within the scope of the claims.

Example: Transdermal patch composition according to the invention:

Colchicine was obtained as gift sample by Watson Pharmaceutical Ltd. Thane, India. Glyceryl Monosterate (GMS) was received from BASF Mumbai, India as a gift sample. Oleic Acid was procured from Hi- Media, Mumbai, India. Ethyl Cellulose, Polyvinyl pyrrolidone was procured from lobachem Pvt Ltd, India. Sodium Laurel Sulphate (SLS), HPLC grade acetonitrile and orthophosphoric acid was procured from Fisher Scientific, Mumbai, India.

Selection of suitable lipids is a preliminary step in formulation of lipoidal nanocarriers based systems like SLNs and NLCs. Various solid lipids (Kolliwax GMS, GMS, Compritol 888, Stearic acid) and liquid lipids viz. Migleol, oleic acid, capric triglycerides, castor oil, were screened for the determination of solubility of drug in them. For the selection of the solid lipid 100mg of drug was placed into 5ml beaker. The solid lipid was added slowly in small increments and beaker was dipped into the water bath to get lipid melted. The temperature was kept 5° C above the melting point of lipids. The lipid was added till the clear lipid is obtained and amount required was determined. Similarly, for determination of solubility of drug in liquid lipids, 100mg of drug was placed in vial and liquid lipids were added slowly in small increments. Each time after addition the mixture was mixed on vortex mixer at 5000rpm for 15 mins. The amount of liquid lipid required to completely dissolve the 100mg of drug was determined.

Selection of proper lipids, surfactant is an essential step during the preparation of Nanostructured Lipid Carriers. Normally entrapment efficiency,

release profile, stability of Nanostructured Lipid Carriers depends on the nature of the lipid selected. Solubility of drug in lipid was utilized as a tool to select solid and liquid lipids. In case of solid lipids the solubility trend was observed as Kolliwax GMS > Creamer GMS > Stearic Acid > Invitor 491 > Invitor 900K > Compritol 888ATO. Similarly for liquid lipids, the solubility pattern was observed as Oleic acid > Castor oil > Migleol > Capric triglyceride. Thus kolliwax GMS and oleic acid were selected as solid and liquid lipid respectively.

While selecting the surfactant the particle size of Nanostructured Lipid Carriers obtained with various surfactants (Viz. Tween 20, Tween 80, Pluornic F68) was taken into consideration. The least particle size was obtained for Tween 20 while it was highest for pluronic F68. The HLB value in between 12 to 16 is best suited for o/w type of emulsion. Tween 20 has HLB within this range (~ 16) while pluronic F68 has value > 24 which is utilized for o/w of emulsion. This may be the reason for getting the different particle size with these surfactants. Thus Tween 20 was selected as a surfactant for studies.

Manufacturing process:

The colchicine nanostructured lipid carriers were prepared by ultrasonication process as. In brief, solid and liquid lipids (lipid phase) were heated (75°C) with constant stirring on magnetic stirrer till the lipids uniformly mix with each other. Colchicine was added in to the lipid mixture and mixed well till it get dissolved in the mixture. In another container surfactant was dissolved in water and heated at 75°C (aqueous phase). The aqueous phase was mixed in the melted lipid phase and both the phases were mixed uniformly by magnetic stirrer at 600 rpm for 10 mins to get OW emulsion. The prepared emulsion was further probe sonicated for 30 mins with 15 sec on-off cycle (75°C). The formulation was placed in the double walled plastic box having the ice cubes. The formulation was sonicated for the next 15 mins for sonication with ice cubes to formulate the colchicine nanostructured lipid carriers. The prepared colchicine nanostructured lipid carriers was purified from unentrapped drug by centrifuging the colchicine loaded. The colchicine loaded nanostructured lipid carriers pellet obtained after centrifugation was

washed twice with phosphate buffer saline to remove further any unentrapped drug attached to the nanostructured lipid carriers. The pellet was then redispersed in phosphate buffer saline and used for further studies. The formulations were stored in 4-8°C till further analysis.

Characterization and Evaluation of colchicine nanostructured lipid carriers

Particle Size, Zeta Potential and Polydispersity Index:

The particle size (z-average diameter), Zeta Potential (Particle Charge) and Polydispersity Index (PDI) were analyzed by Malvern zetasizer. The samples were placed in disposable capillary cuvette and precaution was taken to avoid interference with air bubbles. All samples were analyzed in triplicate.

- The particle size was found to be varying between 120.6 to 97.4nm.
- The PDI value was varied between 0.317 to 0.178.
- The zeta potential was varied within -16.8mV to -25.7mV.

Transmission Electron Microscopy (TEM):

Transmission Electron Microscope was used to examine the physical appearance of prepared nanostructure lipid carriers. The samples were set with negative staining with phosphotungstic acid solution on carbon coated grid and were observed at 10000 to 60000 fold magnification at an increasing speed voltage of 80kV.

The surface of was formed to be smooth and shape was found to be nearly spherical.

X-ray diffraction studies (XRD):

XRD Analysis of pure drug and freeze-dried colchicine nanostructured lipid carriers (10% cryoprotectant manitol) was carried out. The samples were irradiated with monochromatized Cu radiation source and recorded the pattern in between 2θ to 60θ.

Due to entrapment of drug into the lipid matrix which is amorphous in nature, the carriers were observed to be in amorphous form.

Percentage Entrapment Efficiency:

Percentage entrapment efficiency of the prepared colchicine nanostructured lipid carriers was carried out by centrifugation. The formulations were centrifuged at 68250 x g at 4° C for 2hrs. The free (Unentrapped) drug was separated from the formulations (Supernatant). The amount of unentrapped drug was estimated by a validated HPLC method. The percentage entrapment efficiency was calculated by using the following formulae.

$$\text{Percent entrapment efficiency} = \frac{W_a - W_s}{W_a} \times 100 \dots \dots (1)$$

Where,

Wa - Amount of drug initially added

Ws - Amount of drug in supernatant.

The maximum entrapment efficiency was found to be 45.30%

Ex-vivo Skin Permeation Study:

The *ex-vivo* skin permeation study of colchicine nanostructured lipid carriers' emulsion was carried out by using abdominal skin of wistar rats by using Franz diffusion cell having 12 ml capacity receptor compartment. The rat skin was checked for any kind of damage or cut and used. The skin was mounted in between donor and receptor compartment with stratum corneum side facing towards donor compartment using clip. The receptor compartment contains receptor fluids (phosphate buffer saline solution pH 6.4). The temperature of the study was maintained at 37 ± 0.5°C during study with external water bath. The receptor fluid was stirred by 10 × 2.5 mm magnetic stirrer bar. 1mL was placed in the donor compartment. The samples were withdrawn at predetermined time intervals (1, 2, 3, 4, 6, 8, 12, 18, 24, 36 and 48hr) and permeated drug content was analyzed at 245nm by HPLC. The sample volume withdraw was replaced the same volume of fresh phosphate buffer. The permeability coefficients and flux were calculated.

The formulations were showing slow release of drug till 48 hrs. The flux values were found to be in between 6.53 To 11.28 $\mu\text{g}/\text{cm}^2/\text{hrs}$. One of the formulations showed highest flux value of 11.28 $\mu\text{g}/\text{cm}^2/\text{hrs}$.

Skin Permeation by fluorescence microscopy:

To find out the skin penetration potential of colchicine nanostructured lipid carriers Fluorescence Microscopic study was carried out. Colchicine was replaced by Rhodamine B (Rh B) in the NLCs formulation. Wistar rats were used for the study and Rh B- nanostructures lipid carriers formulation was applied on dorsal area. Rats were sacrificed after 6 hours and skin was excised and wiped with tissue paper. Cleaned tissue sample was fixed and prepared the paraffin wax block by standard procedure. Microtomy was used to remove the excess wax and fix the micro ribbon of section on the slide. Fluorescence microscope was used to view the thin sections of samples and images were taken.

The fluorescence photomicrographs of rat skin revealed from the photomicrographs that nanostructures lipid carriers have high transdermal potential as compare to normal Rh B solution. It was proved that the nanostructures lipid carriers have transdermal potential.

Stability Study:

The formulations of colchicine nanostructured lipid carriers were stored at different temperature conditions viz. 4°- 8° C and room temperature for stability studies. After a month the samples were analyzed for particle size and entrapment efficiency. The formulations which were showing good stability with very minute variations in particle size and entrapment efficiency were selected for further study.

Stability study of prepared formulations was carried out at 2-8° C and at room temperature. The particle size and entrapment efficiency were determined at experimental conditions for one month. No any significant change was observed for specified time. Variation in particle size and entrapment efficiency was within the range for both room temperature (RT)

and 4° C (RT, 0.6 – 4.0 % and 1.40 – 5.81 %), (4° C, 0.51 – 3.99 % and 0.33 – 5.52%) respectively, which confirms the stability of preparations at studied environmental conditions. Tween 20 is used as emulsifying agent it is having high HLB value (> 15) and bulky chemical structure with polyoxyethylene chains which may be responsible for steric stabilization. The interaction between sodium lauryl sulphate (anionic surfactant) and cationic lipid may also played role in prevention of aggregation which may have kept particle size constant.

Fabrication and Evaluation of colchicine nanostructured lipid carriers Loaded transdermal patches:

The transdermal patches of colchicine and freeze-dried colchicine nanostructured lipid carriers were prepared by solvent evaporation technique using aluminium foil as backing membrane. On the basis of preliminary screening triethyl citrate (200 µL) was selected as plasticizer while ethyl cellulose and polyvinyl pyrrolidone (8:2) were selected as polymer matrix. The Colchicine was dissolved in the chloroform and colchicine nanostructured lipid carriers in ethanol and plasticizer was added to prepare the dispersion. The dispersion was mixed homogenously by magnetic stirrer at 500rpm for 60 mins. The aluminium foil was placed in petri-dish and dispersion was poured over foil in petri-dish. It was kept overnight for air drying in dust free environment at room temperature. The transdermal patch was evaluated for the various parameters like, weight variation, thickness, folding endurance and drug content.

We claim:

1. A pharmaceutical composition comprising colchicine in the form of transdermal patches, based on Nanostructured Lipid Carriers (NLCs).
2. The composition according to claim 1, wherein the composition comprises pharmaceutically acceptable inert excipients.
3. The composition according to claim 2, wherein the pharmaceutically acceptable inert excipients comprise polymers, plasticizers and solvents.
4. The composition according to claim 1, wherein the lipids are in the form of solid lipids.
5. The composition according to claim 4, wherein the solid lipid is selected from the group consisting of tristearin, stearic acid, cetyl palmitate, cholesterol, glyceryl palmitostearate, glyceryl dibehenate, microcrystalline triglyceride, Bis-Diglyceryl Polyacyladipate, glyceryl monostearate, Glyceryl Stearate Citrate and cetyl alcohol.
6. The composition according to claim 1, wherein the lipids are in the form of liquid lipids.
7. The composition according to claim 6, wherein the liquid lipid is selected from the group consisting of medium chain glycerides, castor oil, capric triglyceride, paraffin oil, 2-octyl dodecanol, oleic acid, squalene, isopropyl myristate, vitamin E and diethylene glycol monoethyl ether.
8. The composition according to claim 1, wherein the lipids are combination of solid lipids and liquid lipids.
9. The composition according to claim 1, wherein the composition is used for the treatment of gout.

10. A process for preparing pharmaceutical composition comprising colchicine in the form of transdermal patches, based on Nanostructured Lipid Carriers (NLCs), the process comprising the steps of:
- a. Preparing the Nanostructured Lipid Carriers comprising solid and liquid lipids; and
 - b. Preparing the transdermal patches using the Nanostructured Lipid Carriers prepared in step (a).

Dated this, 26th April 2018.


()

JOSHI Sumit Ashok

At. Post. Pathare, Taluka
Sinnar, Dist. Nashik, 422104,
Maharashtra, India.

ABSTRACT

The present invention relates to Nanostructured Lipid Carriers (NLCs) based transdermal patches of Colchicine and a process for preparation thereof.

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)  200231612
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Application no:	201821015784
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Filing Date:	26/04/2018
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Amount of Fee Paid:	750/- रुपये एकद/चेक/मनी ऑर्डर द्वारा
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CBR No:	CBR संख्या: 77.5.2.पि. 26/04/2018 के अंतर्गत प्राप्त हुआ
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Signature:	 सिकंदरिया
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1. APPLICANT'S REFERENCE/ IDENTIFICATION NO. (AS ALLOTTED BY OFFICE)	
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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)					
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			Pin Code	422104	
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			Pin Code	590010.	

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			State	Maharashtra
			Country	India
			Pin Code	413531

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]

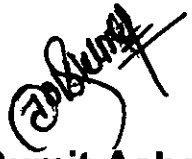
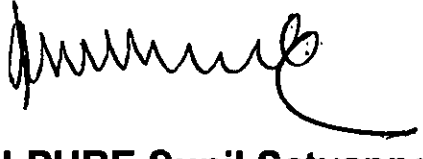



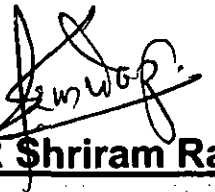
Are all the inventor(s) same as the applicant(s) named above?	Yes (✓)	No ()
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If "NO", furnish the details of the inventor (s) NA

5. TITLE OF THE INVENTION

Nanostructured Lipid Carriers (NLCs) based transdermal patches of Colchicine

6. AUTHORISED REGISTERED	IN/PA No.	N/A
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PATENT AGENT (S)		Name	N/A			
		Mobile No.	N/A			
7. ADDRESS FOR SERVICE OF APPLICANT IN INDIA		Name	JOSHI Sumit Ashok			
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		Telephone No.	NA			
		Mobile no.	07875526666			
		Fax No.	NA			
		E-mail ID	<u>sumit.ajoshi87@gmail.com</u>			
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).						
↓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:	26 th April 2018					
(b) Signature(s):						
(c) Name(s):	<u>JOSHI Sumit Ashok</u>		<u>JALALPURE Sunil Satyappa</u>			
						
	<u>PANCHAL Chandrawadan Vishwambhar</u>		<u>KEMPSWADE Amolkumar Ashok</u>			
						
	<u>VENKATA Siva Naga Malleswara Rao Peram</u>		<u>PETHAKAR Shriram Ramesh</u>			

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26-Apr-2018/193333/201821015784/Form 1

(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 ~~provisional~~/complete 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)	1750	
No. of claim(s)	No. of claims (10) and no. of pages (2)	0	
Abstract	No. of pages (1)	0	

No. of drawing(s)	No. of drawings and No. of pages	N/A	N/A
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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

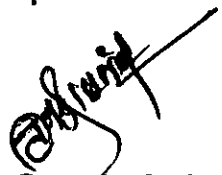
(j).....

Total fee 1750 in cash/ ~~Banker's cheque/Bank Draft bearing No. Date~~ on
~~..... Bank.~~

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

Dated this 26th day of April 2018

Signature:



Name: **JOSHI Sumit Ashok**

At. Post. Pathare, Taluka Sinnar,
Dist. Nashik, 422104, Maharashtra, India.

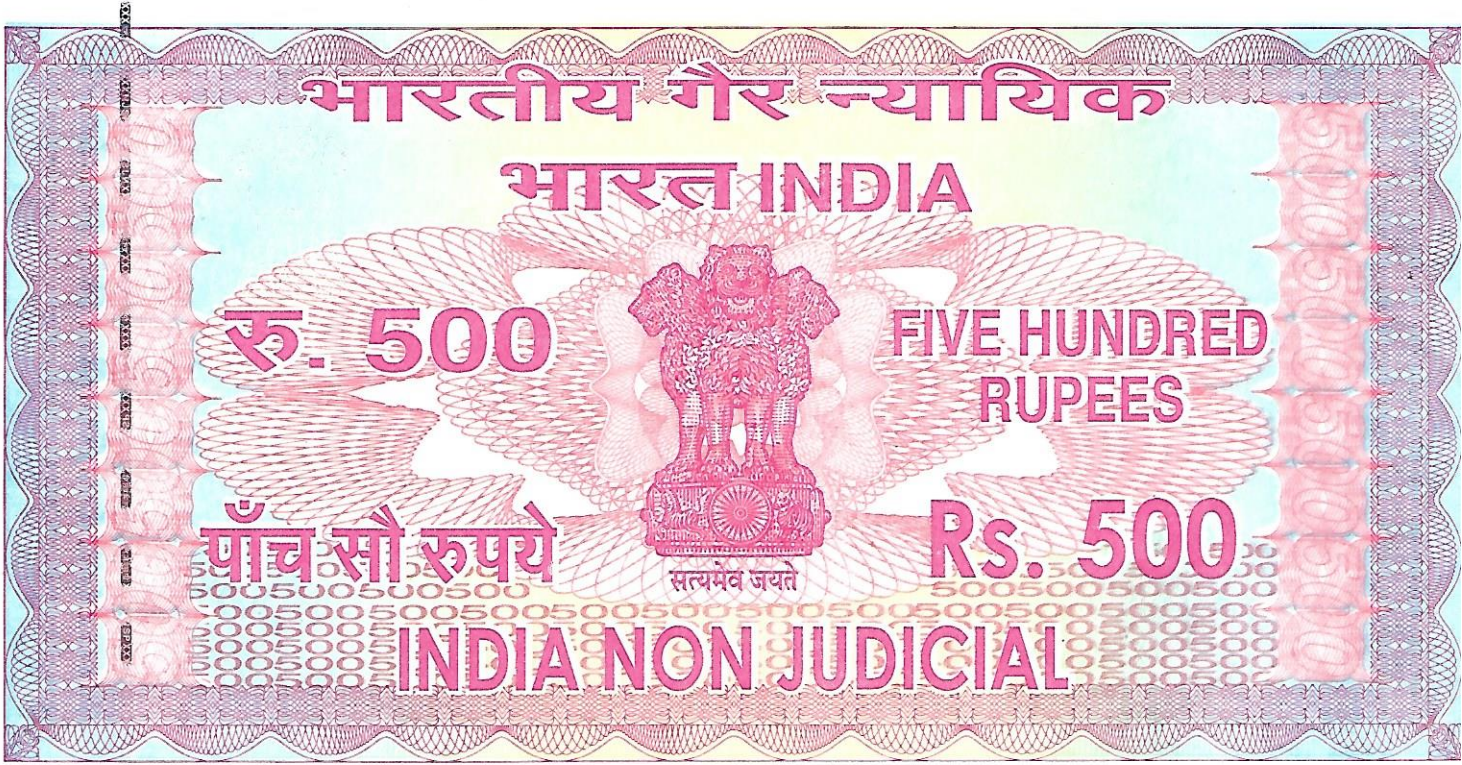
To, The Controller of Patents
The Patent Office, at... **Mumbai**...

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;

26-Apr-2018/19333/201821015784/Form 1

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जिल्हा न्यायालय, लातूर

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)

Power of Attorney 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



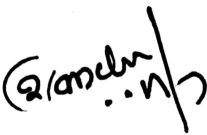



SN	Name	Address
1.	<u>JOSHI Sumit Ashok</u>	At. Post. Pathare, Taluka Sinnar, Dist. Nashik, 422104, Maharashtra, India.
2.	<u>JALALPURE Sunil Satyappa</u>	KLEU's College of Pharmacy and Dr. Prabhakar Kore Basic Science Research Center, KLE University Nehru Nagar, Belagavi, 590010, Karnataka, India.
3.	<u>PANCHAL Chandrawadan Vishwambhar</u>	Maharashtra College of Pharmacy, Nilanga, 413521, Maharashtra, India.
4.	<u>Dr. KEMPSWADE Amolkumar Ashok</u>	Dept. of Pharmaceutics, KLE's College of Pharmacy, Nipani, 591237, Karnataka, India.
5.	<u>VENKATA Siva Naga Malleswara Rao Peram</u>	KLEU's College of Pharmacy and Dr. Prabhakar Kore Basic Science Research Center, KLE University Nehru Nagar, Belagavi, 590010, Karnataka, India.
6.	<u>PETHAKAR Shriram Ramesh</u>	Latur College of Pharmacy, Hasegaon, Taluka Ausa, Dist. Latur, 590010, 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 on 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 authorization, if any made, in respect of, same matter or proceeding.

Dated this 14th day of Oct 2020.

Name	Signature
JOSHI Sumit Ashok	
JALALPURE Sunil Satyappa	
PANCHAL Chandrawadan Vishwambhar	
Dr. KEMPSWADE Amolkumar Ashok	
VENKATA Siva Naga Malleswara Rao Peram	
PETHAKAR Shriram Ramesh	

To,
The Controller of Patents,
The Patent Office
At Mumbai.

FORM 18 THE PATENTS ACT, (39 OF 1970) & The Patents Rules, 2003 REQUEST/EXPRESS REQUEST FOR EXAMINATION OF APPLIATION FOR PATENT	(FOR OFFICE USE ONLY) RQ. No: Filing date: Amount of fee paid: CBR No: Signature:
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1. APPLICANT(S)/ ~~OTHER PERSON~~

SN	Name	Address
1.	<u>JOSHI Sumit Ashok</u>	At. Post. Pathare, Taluka Sinnar, Dist. Nashik, 422104, Maharashtra, India.
2.	<u>JALALPURE Sunil Satyappa</u>	KLEU's College of Pharmacy and Dr. Prabhakar Kore Basic Science Research Center, KLE University Nehru Nagar, Belagavi, 590010, Karnataka, India.
3.	<u>PANCHAL Chandrawadan Vishwambhar</u>	Maharashtra College of Pharmacy, Nilanga, 413521, Maharashtra, India.
4.	<u>Dr. KEMPSWADE Amolkumar Ashok</u>	Dept. of Pharmaceutics, KLE's College of Pharmacy, Nipani, 591237, Karnataka, India.
5.	<u>VENKATA Siva Naga Malleswara Rao Peram</u>	KLEU's College of Pharmacy and Dr. Prabhakar Kore Basic Science Research Center, KLE University Nehru Nagar, Belagavi, 590010, Karnataka, India.
6.	<u>PETHAKAR Shriram Ramesh</u>	Latur College of Pharmacy, Hasegaon, Taluka Ausa, Dist. Latur, 590010, Maharashtra, India.

2. Statement in case of request for examination made by the applicant(s)

I/We hereby request that my/our application for patent no. 201821015784 filed on April 26, 2018 for the invention titled, "NANOSTRUCTURED LIPID CARRIERS (NLCS) BASED TRANSDERMAL PATCHES OF COLCHICINE" shall be examined under sections 12 and 13 of the act.

OR

~~I/We hereby make an express request that my/our application for patent no. _____ filed on _____ based on Patent Cooperation Treaty (PCT) application no. _____ dated _____ made in country _____ shall be examined under sections 12 and 13 of the Act, immediately without waiting for the expiry of 31 months as specified in rule 20(4)(ii).~~

3. Statement in case of request for examination made by any other interested person:

~~I/We the interested person request for the examination of the application no. _____ dated _____ filed by the applicant _____ titled _____~~

~~under sections 12 and 13 of the act.~~

~~As an evidence of my/our interest in the application for patent following documents are submitted.~~

(a) _____

4. ADDRESS FOR SERVICE

Mr. Vijaykumar Shivpuje

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

vijay@patlex.in

Dated this 14th day of October 2020

Shivpuje Vijaykumar Kashinath

IN-PA 1096, Registered Patent Agent

**To, The Controller of Patent,
The Patent office at Mumbai.**

FORM 13

THE PATENTS ACT, 1970 (39 of 1970) and
THE PATENTS RULES, 2003

**APPLICATION FOR AMENDMENT OF THE APPLICATION FOR PATENT/ COMPLETE
SPECIFICATION/ ANY DOCUMENT RELATED THERETO
(See section 57 and Sub-rule (1) of Rule 81)**

We,

SN	Name	Address
1.	<u>JOSHI Sumit Ashok</u>	At. Post. Pathare, Taluka Sinnar, Dist. Nashik, 422104, Maharashtra, India.
2.	<u>JALALPURE Sunil Satyappa</u>	KLEU's College of Pharmacy and Dr. Prabhakar Kore Basic Science Research Center, KLE University Nehru Nagar, Belagavi, 590010, Karnataka, India.
3.	<u>PANCHAL Chandrawadan Vishwambhar</u>	Maharashtra College of Pharmacy, Nilanga, 413521, Maharashtra, India.
4.	<u>Dr. KEMPSWADE Amolkumar Ashok</u>	Dept. of Pharmaceutics, KLE's College of Pharmacy, Nipani, 591237, Karnataka, India.
5.	<u>VENKATA Siva Naga Malleswara Rao Peram</u>	KLEU's College of Pharmacy and Dr. Prabhakar Kore Basic Science Research Center, KLE University Nehru Nagar, Belagavi, 590010, Karnataka, India.
6.	<u>PETHAKAR Shriram Ramesh</u>	Latur College of Pharmacy, Hasegaon, Taluka Ausa, Dist. Latur, 590010, Maharashtra, India.

Request leave to **amend the application/** ~~any document related thereto (Inventors)/ complete specification~~ with respect to application for patent application number 201821015784 filed on 26th April 2018 as highlighted in the copy hereto annexed.

1. Change in the address for service [As per new form 26 submitted]

Mr. Vijaykumar Shivpuje

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

vijay@patlex.in

The reason for making this request are as follows :-

"Fresh form 26 submitted."

We declare that no action for infringement or for the revocation of the patent in question is pending before Appellate Board or a court.

We declare that the facts and matters stated herein are true to the best of our knowledge information and belief.

Dated this 14th day of October 2020.

Shivpuje Vijaykumar Kashinath
IN-PA 1096, Registered Patent Agent

To, The Controller of Patents
The Patent Office, at...**Mumbai**...

We claim:

1. A pharmaceutical composition comprising colchicine in the form of a transdermal patches, ~~based on~~ wherein the transdermal patch is based on a Nanostructured Lipid Carriers (NLCs); wherein the Nanostructured Lipid Carrier is a combination of a solid lipid and a liquid lipid.
2. The composition ~~according to~~ as claimed in claim 1, wherein the composition comprises pharmaceutically acceptable inert excipients.
3. The composition ~~according to~~ as claimed in claim 2, wherein the pharmaceutically acceptable inert excipients ~~comprise~~ is selected from the group consisting of polymers, plasticizers and solvents.
- ~~4. The composition according to claim 1, wherein the lipids are in the form of solid lipids.~~
- 5.4. The composition ~~according to~~ as claimed in claim 4, wherein the solid lipid is selected from the group consisting of tristearin, stearic acid, cetyl palmitate, cholesterol, glyceryl palmitostearate, glyceryl dibehenate, microcrystalline triglyceride, Bis-Diglyceryl Polyacyladipate, glyceryl monostearate, Glyceryl Stearate Citrate and cetyl alcohol.
- ~~6. The composition according to claim 1, wherein the lipids are in the form of liquid lipids.~~
- 7.5. The composition ~~according to~~ as claimed in claim 6, wherein the liquid lipid is selected from the group consisting of medium chain glycerides, castor oil, capric triglyceride, paraffin oil, 2-octyl dodecanol, oleic acid, squalene, isopropyl myristate, vitamin E and diethylene glycol monoethyl ether.
- ~~8. The composition according to claim 1, wherein the lipids are combination of solid lipids and liquid lipids.~~
- ~~9. The composition according to claim 1, wherein the composition is used for the treatment of gout.~~
- 10.6. A process for preparing a pharmaceutical composition comprising colchicine in the form of a transdermal patches, ~~based on Nanostructured Lipid Carriers (NLCs),~~ the process comprising the steps of:

a. ~~Preparing-preparing the a~~ Nanostructured Lipid Carrier (NLC)s comprising solid and liquid lipids; and

b. ~~Preparing-preparing~~ the transdermal patches using the Nanostructured Lipid Carriers prepared in step (a);-

wherein the Nanostructured Lipid Carrier is a combination of a solid lipid and a liquid lipid.

FORM 3

THE PATENTS ACT, 1970

(39 of 1970)

&

THE PATENT RULES, 2003

STATEMENT AND UNDERTAKING UNDER SECTION 8

(See section 8; Rule 12)

1. APPLICANT(S)

Name	Nationality	Address
JOSHI SUMIT ASHOK	Indian	At. Post. Pathare, Taluka Sinnar, Dist. Nashik, 422104, Maharashtra, India

2. NAME, ADDRESS AND NATIONALITY OF THE JOINT APPLICANT

JALALPURE SUNIL SATYAPPA	Indian	KLE College of Pharmacy and Dr. Prabhakar Kore Basic Science Research Center, KLE AHER, Nehru Nagar, Belagavi, 590010, Karnataka, India
PANCHAL CHANDRAWADAN VISHWAMBHAR	Indian	Maharashtra College of Pharmacy, Nilanga, 413521, Maharashtra, India.
KEMPSWADE AMOLKUMAR ASHOK	Indian	Dept. of Pharmaceutics, KLES's College of Pharmacy, Nipani, 591237, Karnataka, India.
VENKATA SIVA NAGA MALLESWARA RAO PERAM	Indian	KLE College of Pharmacy and Dr. Prabhakar Kore Basic Science Research Center, KLE AHER, Nehru Nagar, Belagavi, 590010, Karnataka, India
PETHAKAR SHRIRAM RAMESH	Indian	Latur College of Pharmacy, Hasegaon, Taluka Ausa, Dist. Latur, 413531, Maharashtra, India.

(i) that we have not made any application for the same/substantially the same invention outside India. (**application number 201821015784 dated April 26, 2018**)

OR

(ii) that I/We have made this application No.....dated.....alone/jointly, made for the same/substantially same invention, application(s) for patent in the other countries, the particulars of which are given below:

Name of the country	Date of the application	Application no.	Status of application	Date of Publication/ Publication No.	Date of Grant/ Grant No.
N. A	N. A	N. A	N. A	N. A	N. A

3. NAME AND ADDRESS OF THE ASSIGNEE

(iii) that the rights in the application(s) has/have been assigned to **NONE**.

that I/We undertake that upto the date of 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 day of December, 2020

4. To be signed by the applicant or his authorized registered patent agent.

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

Authorized Agent of Applicant

To,
The Controller of Patents,
The Indian Patent Office,
At Mumbai

DECEMBER 23, 2020

Controller of Patent and Designs,
The Patent Office,
Intellectual Property Office Building,
Antop Hill,
S.M. Road,
Mumbai-400037, India

Kind attention: Dr. Santosh Kumar Samantaray (Controller of Patents)

Re: Indian Patent Application Number: 201821015784 dated April 26, 2018
Applicant: JOSHI SUMIT ASHOK
Title: "NANOSTRUCTURED LIPID CARRIERS (NLCs) BASED TRANSDERMAL PATCHES OF COLCHICINE"

Dear Sir,

This is with reference to the First Examination Report (FER) dated **December 3, 2020** in respect of the captioned matter. Our submissions to the objections raised in the First Examination Report are as follows:

Claim Amendments

Amended claims 1-6 are to replace original claims 1-10. Original claims 4, 6, 8 and 9 are canceled herein without prejudice.

- Amended claim 1 reads as follows:

"A pharmaceutical composition comprising colchicine in the form of a transdermal patches; based on wherein the transdermal patch is based on a Nanostructured Lipid Carriers (NLCs); wherein the Nanostructured Lipid Carrier is a combination of a solid lipid and a liquid lipid."

Support for the above amendments can be found in original claim 8.

- Amended claim 6 reads as follows:

“A process for preparing a pharmaceutical composition comprising colchicine in the form of a transdermal patches, ~~based on Nanostructured Lipid Carriers (NLCs)~~, the process comprising the steps of:

- a. ~~P~~preparing the a Nanostructured Lipid Carrier (NLC) ~~comprising solid and liquid lipids~~; and*
- b. ~~P~~preparing the transdermal patches using the Nanostructured Lipid Carriers prepared in step (a);.*

wherein the Nanostructured Lipid Carrier is a combination of a solid lipid and a liquid lipid.”

Support for the above amendments can be found in original claim 8.

A copy of the amended claim set along with the marked-up copy is enclosed with this response. Applicant further submits that no unsupported subject matter has been added to the claims by way of amendment and that all amendments are completely supported by the specification of the present application.

Our submissions to the objections raised in the First Examination Report in view of the amended claims 1-6 are as follows:

1) NOVELTY

The Ld. Controller has held in the FER, on page 2, that claims 1-10 lack novelty being anticipated in view of disclosure of the following cited document:

D1: S A Joshi et al: "Fabrication and in-vivo evaluation of lipid nanocarriers based transdermal patch of colchicine", Journal of Drug Delivery Science and Technology, vol. 41, 2017, pages 444-453, DOI: 10.1016/j.jddst.2017.08.013.

The Applicant respectfully submits that the cited prior art document, D1, fails to disclose or anticipate the features recited in present claims 1-6.

Discussions that will differentiate the recited features of claims from the disclosure of D1-D5 will now follow in detail:

D1: S A Joshi et al: "Fabrication and in-vivo evaluation of lipid nanocarriers based transdermal patch of colchicine", Journal of Drug Delivery Science and Technology, vol. 41, 2017, pages 444-453, DOI: 10.1016/j.jddst.2017.08.013.

D1 relates to formulation and evaluation of Solid Lipid Nanoparticles (SLNs) based transdermal patch of colchicine. D1 discloses preparation of Colchicine loaded SLNs (C-SLNs) prepared by ultrasonication method and optimized with respect to the concentration of lipid and surfactant by 3² full factorial design. D1 also discloses the use of SLNs based transdermal patch of colchicine for the treatment of gout. D1 at best discloses the use of solid lipids like Kolliwax GMS, GMS, Compritol 888 and Stearic acid.

However, S1 is completely silent on the use of liquid lipid (eg. castor oil, capric triglyceride, paraffin oil, 2-octyl dodecanol, oleic acid, squalene, isopropyl myristate, vitamin E and diethylene glycol monoethyl ether) in the transdermal patch of colchicine.

Since D1 is silent on liquid lipid, it cannot possibly disclose a colchicine transdermal patch, wherein the Nanostructured Lipid Carrier (NLC) is a combination of a solid lipid and a liquid lipid as required by amended claim 1 and claim 6.

Therefore, D1 fails to disclose all the features recited in claim 1 and claim 6 and cannot be considered a novelty destroying document.

Further, dependent claims 2-5 dependent directly or indirectly on claim 1. Hence, dependent claims 2-5 are also novel at least by virtue of their dependency on claim 1. Accordingly, the Ld. Controller is requested to waive the object.

2) INVENTIVE STEP

The Ld. Controller has held in the FER, on page 2, that claims 1-10 lack inventive step, being obvious in view of the teaching (s) of the following cited documents:

- **D1: Quantitative analysis of adenosine using Liquid Chromatography/Atmospheric Pressure Chemical Ionization - tandem Mass Spectrometry (LC/APCI-MS/MS), Annelies Van Dycke, et. al , J Chromatogr B Analyt Technol Biomed Life Sci.**
- **D2: WO 2012/176212 A4**

- **D3: H P Singh et al: "Elastic liposomal formulation for sustained delivery of colchicine: in vitro characterization and in vivo evaluation of anti-gout activity", The AAPS journal, vol. 11, no. 1, 2009, pages 54-64, DOI:10.1208/s12248-008-9078-8.**
- **D4: B V Bonifacio et al: "Nanotechnology-based drug delivery systems and herbal medicines: a review",International Journal of Nanomedicine, vol. 9(1), 2014, pages 1-15, DOI: 10.2147/IJN.S52634.**
- **D5: WO 2013/166498 A1**

The Applicant respectfully submits that D1-D5, whether taken singularly or in combination, fail to teach or suggest the recited features of claims 1-6.

Technical effect

The present invention relates to a transdermal patch for treatment of Gout that is based on a Nanostructured Lipid Carriers (NLCs). NLCs are next generation of the lipid nanoparticles. NLCs are modified SLNs in which lipidic phase is contained both solid (fat) and liquid (oil) lipids at ambient temperature. In fact, NLCs are modified generations of SLNs that presenting a mixture of solid and liquid phase (oil) forming a formless matrix, which improves the stability and capacity loading. NLCs show contrasts with SLNs: more loading capacity for some drugs, some less water in the dispersion, prevent or minimize the drug expulsion during storage, but not reported significant difference between the biotoxicity of SLNs and NLCs. Further, the NLCs improve the bioavailability of the colchicine and have less toxicological risk owing to the natural and biological origins of the materials.

Discussions that will differentiate the recited features of claims from the disclosure of D1-D5 will now follow in detail:

D1:Quantitative analysis of adenosine using Liquid Chromatography/Atmospheric Pressure Chemical Ionization - tandem Mass Spectrometry (LC/APCI-MS/MS), Annelies Van Dycke, et. al , J Chromatogr B Analyt Technol Biomed Life Sci.

D1 discloses a formulation and evaluation of solid lipid nanoparticles (SLNs) based transdermal patch of colchicine. Preparation of colchicine loaded SLNs (C-SLNs) by ultrasonication method and optimization with respect to the concentration of lipid and surfactant are also elaborated in D1. D1 also discloses an improvement in the bioavailability of the

colchicine by incorporating it in SLNs based transdermal patch and to evaluate their *in vivo* anti-gout potential in rats by monosodium urate induced subcutaneous air pouch model.

However, the colchicine loaded Solid Lipid Nano particles (SLNs) used in D1 are different from nanostructured lipid carriers (NLCs) used in present claim 1 and claim 6. NLCs are modified SLNs in which lipidic phase is contained both solid (fat) and liquid (oil) lipids at ambient temperature. NLCs are modified generations of SLNs that presenting a **mixture of solid and liquid phase (oil)** forming a formless matrix, which improves the stability and capacity loading. NLCs show contrasts with SLNs: more loading capacity for some drugs, some less water in the dispersion, prevent or minimize the drug expulsion during storage. Please see lines 26- 31 on page 4 and lines 1-2 on page 5.

Since, D1 is completely silent about liquid lipids, it cannot teach or suggest the NLC of present claim 1 and claim 6 which is combination of both solid and liquid lipid.

Given the above, the Applicant submits that D1 cannot motivate the person of ordinary skill in the art to combine solid lipid with liquid lipid to reach at the composition of claim 1 and claim 6.

Hence, D1, alone or in combination, does not motivate the person skilled in the art to arrive at the recited features of independent claim 1 and claim 6.

D2: WO 2012/176212 A4

D2 does not cure the deficiency of D1. D2 relates to a lipid nano carrier based nanogel formulation comprising at least one active agent, a lipid, surfactant, hydrophilic polymer, alkalizing agent, cryoprotectant, buffer, preservative, anti-oxidant, hydrating fluid and pharmaceutically acceptable additives. D2 discloses use of phospholipids like phosphatidylcholine, egg phosphatidylcholine, disteryl phosphatidyl choline, phosphatidylethanolamine, phosphatidylserine. D2 discloses the said active ingredient comprises a hydrophilic drug selected from a group 5 -fluorouracil (5-FU), acyclovir, colchicine, diclofenac and glucosamie. D2 further discloses the said formulation has a good local bioavailability.

However, D2 fails to disclose, teach or suggest the nanostructured lipid carriers (NLCs) used in present claim 1, wherein the lipidic phase contains both solid (fat) and liquid (oil) lipids. D2 discloses the lipids in the nano carriers to be solid phospholipids which are different from

the solid lipids used in the present invention. D2 fails to disclose any liquid lipid in the nanocarriers. Furthermore, D2 is a nanogel composition in contrast to composition of present claim1 which relates to a transdermal patch.

D2 mainly discloses lipid nano carrier based nanogel formulation comprising 5-FU. D2 just mentions colchicine as one of the choices for active ingredients but does not disclose any specific composition of colchicine with lipid carriers in any example.

Since, D2 like D1 is completely silent about liquid lipids, it cannot teach or suggest the NLC of present claim 1 and claim 6 which is combination of both solid and liquid lipid.

Given the above, the Applicant submits that D2 cannot motivate the person of ordinary skill in the art to combine solid lipid with liquid lipid to reach at the composition of claim 1 and claim 6.

Hence, D2, alone or in combination, does not motivate the person skilled in the art to arrive at the recited features of independent claim 1 and claim 6.

D3: H P Singh et al: "Elastic liposomal formulation for sustained delivery of colchicine: in vitro characterization and in vivo evaluation of anti-gout activity", The AAPS journal, vol. 11, no. 1, 2009, pages 54-64, DOI:10.1208/s12248-008-9078-8

D3 does not cure the deficiency of D1 and D2. D3 relates to development and *in vitro* and *in vivo* evaluation of elastic liposomal formulation for topical delivery of colchicine. D3 discloses the elastic liposomal formulation of colchicine to have greater potential to enhance skin accumulation, prolong drug release, and improve the site-specificity of colchicine. D3 at best discloses anti -gout activity of said formulation on monosodium urate-induced air pouch model.

However, delivery system disclosed in D3 is based on Elastic Liposomal Formulation for sustained delivery of Colchicine which is completely different from the composition disclosed in present claim1. D3 discloses the elastic liposome formed of phospholipid i.e. Soya phosphatidylcholine (PC) (Please refer to materials and method section of D3) and gives no hint about nanostructured lipid carriers (NLCs) based transdermal patch of colchicine which is combination of both solid and liquid lipids. Further, D3 does not give any hint about formulating colchicine in the form of transdermal patch. Hence, D3 fails to disclose, teach or suggest the NLC based transdermal patch of colchicine as recited in claim1 and claim 6.

Since D3 does not give any hint about NLCs, D3 cannot motivate the person of ordinary skill in the art to use nanostructured lipid carriers (NLCs) based system for transdermal delivery of colchicine as required by claim 1 and claim 6.

Hence, D3, alone or in combination with D1 and D2, does not motivate the person skilled in the art to arrive at the recited features of independent claim 1 and claim 6.

D4: B V Bonifacio et al: "Nanotechnology-based drug delivery systems and herbal medicines: a review", International Journal of Nanomedicine, vol. 9(1), 2014, pages 1-15, DOI: 10.2147/IJN.S52634

D4 is a state of the art review article regarding nanotechnology-based drug delivery systems for herbal medicines. D4 discloses various nanotechnology based drug delivery systems, such as polymeric nanoparticles, solid lipid nanoparticles (SLNs), liquid crystal (LC) systems, precursor systems for liquid crystals (PSLCs), liposomes, and microemulsions to improve a formulation's most desirable properties. D4 also discloses about Nanostructured lipid carriers (NLCs) based delivery system and methods used to produce NLCs, including high-pressure homogenization, emulsification-sonication, microemulsion and solvent emulsification-evaporation techniques. D4, at best mentions about incorporation of natural flavonoid Quercetin into NLCs (QU-NLCs), to evaluate the formulation's potential as a topical delivery system in a study by Guo et al.

However, D4 is completely silent about colchicine and its anti gout activity. D4 also does not give hint about formulating any herbal drug in the form of a transdermal patch based on NLCs as required by present claim 1 and claim 6.

Furthermore, there are wide variety of biologically active constituents available from herbal plants which not only vary in structure but also properties. So, selection of suitable transdermal delivery system and selection of appropriate solid and liquid lipids (for NLC) that is suitable for a particular drug requires lot of research and experimentation and cannot be considered as obvious based on general disclosure in the state of the art.

Since, D4 is silent about colchicine and transdermal patches, D4 possibly cannot teach or suggest any person of ordinary skill in the art to formulate the transdermal patch of colchicine by utilizing nano structured lipid carrier (NLC) of claim 1 and claim 6.

Hence, D4, alone or in combination with D1-D3, does not motivate the person skilled in the art to arrive at the recited features of independent claim 1 and claim 6.

D5: WO 2013/166498 A1

D5 relates to mucus penetrating liposomal nanoparticles comprising one or more PEG-conjugated lipids, one or more lipids, and one or more therapeutic, prophylactic, and/or diagnostic agents.

However, liposomal nanoparticles disclosed in D5 are completely different from the nano structured lipid carrier (NLC) disclosed in present claim 1 and claim 6. The "Liposome" refers to vesicles or particles which possess a lipid bilayer enclosing an aqueous compartment and are prepared by methods completely different from that disclosed in present invention. D5 discloses the use of phospholipids particularly phosphatidylcholine, phosphatidylethanolamine etc. which are different from solid and liquid lipids used in present invention. Hence, D5 is completely silent on NLC of claim 1 and claim 6. Further, D5 relates to mucus penetrating nanoparticles and does not give any hint about transdermal mode of delivery.

Since, D5 is completely silent on nanostructured lipid carriers (NLCs) and does not teach or suggest any transdermal mode of delivery, D5 cannot motivate a person skilled in the art to formulate the transdermal patch of colchicine by utilizing nano structured lipid carrier (NLC) of claim 1 and claim 6.

Hence, D5, alone or in combination with D1-D4, does not motivate the person skilled in the art to arrive at the recited features of independent claim 1 and claim 6.

Further, dependent claims 2-5 dependent directly or indirectly on claim 1. Hence, dependent claims 2-5 are also inventive at least by virtue of their dependency on claim 1. Accordingly, the Ld. Controller is requested to waive the object.

3) NON-PATENTABILITY

The Ld. Controller, on page 4, in the FER has held that "[c]laims 1-10 of the alleged application falls within the scope of such clause (e) of section 3 of the Patent Act, as it appears that the claimed pharmaceutical composition comprising nanostructured lipid carriers (NLCs) based transdermal patch of colchicine is a mere admixture with no

evidence of synergism provided in the specification and its process for preparation thereof..”

The Applicant respectfully disagrees and submits that Independent claim 1 is not an admixture. The claim 1 refers to a dosage form i.e nanostructured lipid carriers (NLCs) based transdermal patch of colchicine. The composition is not meant to achieve synergism among components. but relates to physical form of a dose of colchicine intended for administration or consumption.

Without acquiescing, if composition of claim 1 is considered to be an admixture, the NLCs of claim 1 exhibit synergistic effect like more loading capacity for some drugs, some less water in the dispersion, prevent or minimize the drug expulsion during storage and improve the bioavailability of the colchicine and have less toxicological risk owing to the natural and biological origins of the materials.

Further, independent claim 6 is not an admixture but relates to a process/ method of preparation of nanostructured lipid carriers (NLCs) based transdermal patch of colchicine. Hence, independent claim 1 and claim 6 will not attract section 3 (e). Accordingly, the Ld. Controller is requested to waive off the objection.

4) SUFFICIENCY OF DISCLOSURE:

a) The Ld. Controller, on page 4, in the FER has held that “[t]he application does not sufficiently define the invention because the application does not disclose the invention in a manner that is sufficiently complete for it to be carried out by the skilled person. The amount of the active ingredient, i.e., colchicine, lipid and excipients in the form of nanostructured lipid carriers (NLCs) based transdermal patch are not disclosed in the claims which is a crucial factor in such drug delivery systems.”

The Applicant respectfully disagrees and submits that the claims are always read in light of the specification. A person of ordinary skill in the art after reading the claims and other necessary details mentioned in the example of the present specification (Please refer page 12, 13 and 14 of present specification), can easily arrive at the nanostructured lipid carriers (NLCs) based transdermal patch of colchicine. Accordingly, the Ld. Controller is requested to waive off the objection.

The lipids are also broadly defined and specific solid lipid/ liquid lipid as claimed in dependent claims extend beyond what is actually tested in working examples.

The Applicant respectfully disagrees and submits that the example mentioned in the present specification mentions most of the specific solid and liquid lipids mentioned in dependent claims 4 and 5 respectively. For the purpose of selection of suitable lipids in the NLC based formulation various solid lipids (Kolliwax Glyceryl Monostearate (GMS), Creamer GMS, Compritol 888 (Glyceryl behenate), Stearic acid) and liquid lipids viz. Migleol, oleic acid, capric triglycerides, castor oil, were screened for the determination of solubility of drug in them. Please refer lines 1-8 on page 13 of specification. However, there is no requirement to test each and every lipid mentioned in dependent claims and it is sufficient to test few representative members for the purpose of enablement. Accordingly, the Ld. Controller is requested to waive off the objection.

Furthermore, the application does not demonstrate anything unexpected such as synergy between the components of the claimed composition comprising nanostructured lipid carriers (NLCs) based transdermal patch of colchicine. The present claims therefore lack support and the application so lacks sufficiency of disclosure within the meaning of section 10(4) of the Patents Act."

The Applicant respectfully disagrees and submits that the nanostructured lipid carriers (NLCs) based transdermal patch of colchicine of claim 1 exhibit synergistic effect like more loading capacity for some drugs, some less water in the dispersion, prevent or minimize the drug expulsion during storage and improve the bioavailability of the colchicine and have less toxicological risk owing to the natural and biological origins of the materials. Accordingly, the Ld. Controller is requested to waive off the objection.

b) Source and geographical origin of the biological material, i.e., Colchicine, Castor oil should be disclosed in the complete specification u/s 10(4)(ii)(D) of the Patents Act.

The Applicant respectfully disagrees and submits that the biological materials used in the present invention have been procured commercially. The geographical origin of biological material used in the specification is mentioned in lines 8-13 of page 12 of specification. Accordingly, the Ld. Controller is requested to waive off the objection.

5) CLARITY AND CONCISENESS

Claim 9 refers to the expression "used for the treatment of gout" which recites intended therapeutic use of the claimed composition. This so called result-to-be-achieved type of

definition renders the subject-matter claimed unclear.

The Applicant submits that claim 9 has been cancelled without prejudice. Hence, the objection stands moot in view of the cancellation. Accordingly, Ld. Controller is requested to waive the above objection.

6) National Biodiversity Act (NBA) Approval

Attention of the applicant is invited towards Section 6 of the Biodiversity Act 2002 which mandates that if biological material obtained from India is used in the application for Patent, then permission and other information for making application for patent should be obtained from the National Biodiversity Authority and details should be furnished in the application Form 1 column 9 (iii).

The Applicant submits that all the biological material used in the present invention (colchicine, castor oil etc.) has been procured commercially. Colchicine was obtained as gift sample by Watson Pharmaceutical Ltd. Thane, India. Glyceryl Monosterate (GMS) was received from BASF Mumbai, India as a gift sample. Oleic Acid was procured from Hi- Media, Mumbai, India. Please, refer to example on page 12. Hence, the biological materials used in present invention are not obtained directly from plants but obtained by commercial means.

Section 7 of the Biological Diversity Act, 2002 requires that any entity whether any Indian person, India private limited or public limited companies or any foreign person or foreign company needs to give a prior intimation to the respective State Biodiversity Board (SBB) for obtaining biological resource from its territory for commercial utilization.

Hence, the companies commercializing the biological materials used in the present invention must have already taken permission and have entered into a benefit sharing agreement with the NBA before commercial utilization of said biological materials.

Hence, there is no requirement to take NBA permission twice for same biological materials. Accordingly, the Ld. Controller is requested to waive off the objection.

The expression “according to claim(s)” should be replaced with “as claimed in claim(s)” in dependent claims.

The Applicant submits that dependent claims have been suitably amended to replace the phrase “according to claim(s)” with “as claimed in claim(s)”. Accordingly, the Ld. Controller is requested to waive off the objection.

8) FORMAL REQUIREMENTS

a) Details regarding application for patents which may be filed outside India from time to time for the same or substantially the same invention should be furnished within six months from the date of filing of the said application under clause (b) of sub section (1) of section 8 and rule 12(2) of the Patents Act and Rules.

Regarding the objection, the Applicants submits that a Form-3 has been submitted at IPO at the time of filing of application April 26, 2018 stating that no application has been filed for the same or substantially the same invention outside India. The Applicant has not filed any patent Application outside India till date. We are submitting a fresh Form-3 stating the same. Accordingly, the Ld. Controller is requested to take the same on record and waive off the objection.

b) Details regarding the search and/or examination report including claims of the application allowed, as referred to in Rule 12(3) of the Patent Rule, 2003, in respect of same or substantially the same invention filed in all the major Patent offices along with appropriate translation where applicable, should be submitted within a period of six months from the date of receipt of this communication as provided under section 8(2) of the Indian Patents Act.

The Applicant submits that no application has been filed for the same or substantially the same invention outside India. Accordingly, the Ld. Controller is requested to waive off the objection.

c)The Applicant is required to obtain permission from the National Biodiversity Authority u/s 6 of the Biodiversity Act because the Applicant has used biological materials such as Colchicine, Castor oil obtained from India.

The Applicant submits that all the biological material used in the present invention (colchicine, castor oil etc.) has been procured commercially. Colchicine was obtained as gift sample by Watson Pharmaceutical Ltd. Thane, India. Glyceryl Monosterate (GMS) was received from BASF Mumbai, India as a gift sample. Oleic Acid was procured from Hi- Media, Mumbai, India.

Please, refer to example on page 12. Hence, the biological materials used in present invention are not obtained directly from plants but obtained by commercial means.

Hence, the companies commercializing the biological materials used in the present invention must have already taken permission and have entered into a benefit sharing agreement with the NBA before commercial utilization of said biological materials.

Hence, there is no requirement to take NBA permission twice for same biological materials. Accordingly, the Ld. Controller is requested to waive off the objection.

d) Format of Specification (rule13): Abstract should commence with the title of the invention u/r 13(7)(a) of the Patents Rules.

With regard to the objection, the Applicant submits that a fresh Abstract in accordance with section 13(7) mentioning the title has been filed at the IPO. Accordingly, the Ld. Controller is requested to take the same on record and waive off the objection.

e) Other Deficiencies:

Indian patent application number should be duly mentioned in Form 3 and Form 5.

The Applicant submits that updated Forms 3 and 5 mentioning the Indian patent application number are submitted at the IPO. Accordingly, the Ld. Controller is requested to take the same on record and waive off the objection.

In view of the above submissions and amendments, it is submitted that all objections raised by the Ld. Controller has been complied with and the application is in order for grant. The Ld. Controller is further requested to allow an opportunity to be heard in the matter before passing any adverse orders.

Signature:

Digitally signed by,

Name:

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. APPLICANT(S)

Name	Nationality	Address
JOSHI SUMIT ASHOK	Indian	At. Post. Pathare, Taluka Sinnar, Dist. Nashik, 422104, Maharashtra, India
JALALPURE SUNIL SATYAPPA	Indian	KLE College of Pharmacy and Dr. Prabhakar Kore Basic Science Research Center, KLE AHER, Nehru Nagar, Belagavi, 590010, Karnataka, India
PANCHAL CHANDRAWADAN VISHWAMBHAR	Indian	Maharashtra College of Pharmacy, Nilanga, 413521, Maharashtra, India.
KEMPWADE AMOLKUMAR ASHOK	Indian	Dept. of Pharmaceutics, KLES's College of Pharmacy, Nipani, 591237, Karnataka, India.
VENKATA SIVA NAGA MALLESWARA RAO PERAM	Indian	KLE College of Pharmacy and Dr. Prabhakar Kore Basic Science Research Center, KLE AHER, Nehru Nagar, Belagavi, 590010, Karnataka, India
PETHAKAR SHRIRAM RAMESH	Indian	Latur College of Pharmacy, Hasegaon, Taluka Ausa, Dist. Latur, 413531, Maharashtra, India.

hereby declare that the true and first inventor(s) of the invention disclosed in the complete specification filed in pursuance of our application number: **201821015784** dated **April 26, 2018** are:

2. INVENTOR(S)

Name	Nationality	Address
JOSHI SUMIT ASHOK	Indian	At. Post. Pathare, Taluka Sinnar, Dist. Nashik, 422104, Maharashtra, India
JALALPURE SUNIL SATYAPPA	Indian	KLE College of Pharmacy and Dr. Prabhakar Kore Basic Science Research Center, KLE AHER, Nehru Nagar, Belagavi, 590010, Karnataka, India
PANCHAL CHANDRAWADAN VISHWAMBHAR	Indian	Maharashtra College of Pharmacy, Nilanga, 413521, Maharashtra, India
KEMPWADE AMOLKUMAR ASHOK	Indian	Dept. of Pharmaceutics, KLES's College of Pharmacy, Nipani, 591237, Karnataka, India.

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PETHAKAR SHRIRAM RAMESH	Indian	Latur College of Pharmacy, Hasegaon, Taluka Ausa, Dist. Latur, 413531, Maharashtra, India.

3. DECLARATION TO BE GIVEN WHEN THE APPLICATION IN INDIA IS FILED BY THE

APPLICANT(S) IN THE CONVENTION COUNTRY: -

We the applicant(s) in the convention country hereby declare that our right to apply for a patent in India is by way of assignment from the true and first inventor(s).

Dated this day of, 2020

Vijaykumar Shivpuje, IN/PA 1096,

Sri Kripa, Akshay Nagar,

Old Ausa Road, Latur, 413531,

Maharashtra, India

Authorized Agent of Applicant

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 day of, 2020

To,

The Controller of Patents,

The Indian Patent Office, Mumbai

We claim:

1. A pharmaceutical composition comprising colchicine in the form of a transdermal patch; wherein the transdermal patch is based on a Nanostructured Lipid Carrier (NLC); wherein the Nanostructured Lipid Carrier is a combination of a solid lipid and a liquid lipid.
2. The composition as claimed in claim 1, wherein the composition comprises pharmaceutically acceptable inert excipients.
3. The composition as claimed in claim 2, wherein the pharmaceutically acceptable inert excipients is selected from the group consisting of polymers, plasticizers and solvents.
4. The composition as claimed in claim 4, wherein the solid lipid is selected from the group consisting of tristearin, stearic acid, cetyl palmitate, cholesterol, glyceryl palmitostearate, glyceryl dibehenate, microcrystalline triglyceride, Bis-Diglyceryl Polyacyladipate, glyceryl monostearate, Glyceryl Stearate Citrate and cetyl alcohol.
5. The composition as claimed in claim 6, wherein the liquid lipid is selected from the group consisting of medium chain glycerides, castor oil, capric triglyceride, paraffin oil, 2-octyl dodecanol, oleic acid, squalene, isopropyl myristate, vitamin E and diethylene glycol monoethyl ether.
6. A process for preparing a pharmaceutical composition comprising colchicine in the form of a transdermal patch , the process comprising the steps of:
 - a. preparing a Nanostructured Lipid Carrier (NLC) ; and
 - b. preparing the transdermal patches using the Nanostructured Lipid Carrier prepared in step (a);wherein the Nanostructured Lipid Carrier is a combination of a solid lipid and a liquid lipid.



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व्यापार चिह्न/TRADE MARKS|भौगोलिक
उपदर्शन/GEOGRAPHICAL INDICATIONS



सत्यमेव जयते
भारत सरकार
GOVERNMENT OF INDIA

एकस्व कार्यालय /THE PATENT OFFICE
बौद्धिक सम्पदा भवन / I.P.O. BUILDING
एंटाप हिल/Antop Hill,
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ई मेल/ Email: mumbai-patent@nic.in
वेबसाइट /Website: <http://ipindia.nic.in>

सं.संख्या/Ref.No /आवेदन संख्या/Application No/ 201821015784

दिनांक/Date of Dispatch/Email: 03/12/2020

सेवा मे,/To

JOSHI SUMIT ASHOK,
JOSHI SUMIT ASHOK AT. POST. PATHARE, TALUKA SINNAR, DIST. NASHIK-422 104, MAHARASHTRA,
INDIA.

Email : sumit.ajoshi87@gmail.com, vijay@patlex.in

विषय: एकस्व अधिनियम, 1970 की धारा 12 व 13 तथा एकस्व नियम, 2003 के अधीन परीक्षण रिपोर्ट

Subject: Examination report under sections 12 & 13 of the Patents Act, 1970 and the Patents Rules, 2003.

1. उपर्युक्त आवेदन के संदर्भ में परीक्षण रिपोर्ट (अर्थात्, एकस्व नियम, 2003 (यथा संशोधित) के नियम 24-ख(3) में विनिर्दिष्ट आपत्तियों का प्रथम कथन) इसके साथ संलग्न है। यह रिपोर्ट परीक्षण हेतु अनुरोध दिनांक 14/10/2020 के उत्तर में जारी की गयी है। परीक्षण रिपोर्ट का उत्तर दाखिल करने की अंतिम तिथि (अर्थात्, इस रिपोर्ट में लगाई गयी सभी आवश्यकताओं के अनुपालन की अवधि) आवेदक को आपत्तियों का प्रथम कथन जारी होने की तिथि से छः माह है।

Please find enclosed herewith an Examination Report (i.e. a first statement of objections as specified in Rule 24-B(3) of The Patents Rules, 2003 (as amended)) in respect of above-mentioned application. This report is issued with reference to a request for examination dated 14/10/2020. The last date for filing a response to the Examination Report (i.e. a period to comply with all the requirements raised in this examination report) is six months from the date on which the first statement of objections is issued to the Applicant.

2. यदि रिपोर्ट के अंतर्गत लगाई गयी आवश्यकताओं का अनुपालन एकस्व नियम, 2003 (यथा संशोधित) के नियम 24 ख(5) में विनिर्दिष्ट अवधि के भीतर अंदर अनुपालन नहीं किया गया तो एकस्व अधिनियम 1970 की धारा 21(1) के अधीन वर्तमान आवेदन को परित्यक्त माना जाएगा।
The instant application shall be deemed to have been abandoned under Section 21(1) of The Patents Act, 1970, unless all the requirements raised in this report are complied with in the period as specified in Rule 24-B (5) of The Patents Rules, 2003 (as amended).
3. आपका ध्यान एकस्व नियम, 2003 के नियम 24 ख(6) के प्रावधानों की ओर भी आमंत्रित किया जाता है।
Your attention is also invited to the provisions of Rule 24-B (6) of the Patents Rules 2003.
4. आपको सलाह दी जाती है कि शीघ्र निपटान हेतु अपना उत्तर शीघ्र प्रस्तुत करें।
You are advised to file the reply at the earliest for early disposal.

Dr. Santosh Kumar Samantaray
नियंत्रक पेटेंट/ Controller of Patents

संलग्न/Enclosed: अपरोक्त अनुसार/As above

टिप्पणी: यह इलेक्ट्रॉनिक रूप से उत्पन्न रिपोर्ट है।

NOTE: This is an electronically generated report.

सभी पत्राचार नियंत्रक एकस्व को उपरोक्त लिखित पते पर भेजा जाये।

All communications should be sent to the Controller of Patents at the above mentioned address.

परीक्षण रिपोर्ट / Examination Report

आवेदन संख्या /Application Number	201821015784
दाखिल करने की तिथि /Date of Filing	26/04/2018
पूर्विका दिनांक /Date of Priority	--
पीसीटी अंतर्राष्ट्रीय आवेदन की संख्या व दिनांक / PCT International Application No. & Date	--
आवेदक /Applicant	KEMPWADE AMOLKUMAR ASHOK
परीक्षण हेतु अनुरोध की संख्या व दिनांक /Request for Examination No. & Date	R20202032131 14/10/2020
प्रकाशन की तिथि /Date of Publication	22/06/2018

इस परीक्षण रिपोर्ट के चार भाग हैं, अर्थात रिपोर्ट का सारांश, विस्तृत तकनीकी रिपोर्ट, औपचारिक आवश्यकताएँ तथा रिकॉर्ड में दस्तावेज़ /
This examination report consists of four parts, namely summary of the report, detailed technical report, formal requirements and documents on record.

भाग -1: रिपोर्ट का सारांश

PART-I: SUMMARY OF THE REPORT

क्र. सं. /Sl. No.	अधिनियम के तहत आवश्यकताओं पर विस्तृत टिप्पणियाँ /Requirements under the Act	दावों की संख्या /Claim Numbers	टिप्पणी /Remarks
1.	नवीनता /Novelty	दावे /Claims:	हाँ /Yes
		दावे /Claims: 1-10	नहीं /No
	आविष्कारी कदम / Inventive step	दावे /Claims:	हाँ /Yes
		दावे /Claims: 1-10	नहीं /No
औद्योगिक उपयोगिता /Industrial Applicability	दावे /Claims: 1-10	हाँ /Yes	
	दावे /Claims:	नहीं /No	
2.	धारा 3 के अधीन पेटेंट-अयोग्यता (यदि हाँ, खंड 3(क-त) /Non-patentability u/s 3 (if yes, specify section 3(a-p))	दावे /Claims: 1-10	हाँ /Yes e
		दावे /Claims:	नहीं /No
3.	धारा 10(4) के अधीन प्रकटन की दक्षता (हाँ/नहीं निर्दिष्ट करें) /Sufficiency of disclosure u/s 10 (4) (Specify Yes/No)	No	
4.	[धारा 10(5) व 10(4) (ग)] के अधीन दावे /Claims [u/s 10(5) & 10(4) (c)] स्पष्टता/ संक्षिप्तता /Clarity / Conciseness	दावे /Claims:	हाँ /Yes
		दावे /Claims: 9	नहीं /No

भाग -II विस्तृत तकनीकी रिपोर्ट

PART-II: DETAILED TECHNICAL REPORT

क. उद्धरित दस्तावेजों की सूची /A.List of documents cited:

(क) पेटेंट साहित्य / (a). Patent Literature :

क्र. सं. / Sl.no	दस्तावेजों का विवरण /Details of documents	प्रकाशन तिथि(दिन/माह/वर्ष) / Publication date	उद्धरित दस्तावेज का प्रासंगिक विवरण (पृष्ठ व अनुच्छेद संख्या) / Relevant description (page and paragraph no.) of cited document	उद्धरित दस्तावेज के प्रासंगिक दावे / Relevant claims of cited document	अभिकथित आविष्कार के दावे /Claims of alleged invention
	WO 2012/176212				

1	WO 2012/170212 A4	27/12/2012	abstract	Claims 1-3, 5	1-10
2	WO 2013/166498 A1	07/11/2013	page 2, line 18-page 3, line 8; page 22, lines 17- 20	Claim 1-20	1-10

(ख) गैर-पेटेंट साहित्य /(b).Non-patent literature

क्र. सं. /Sl.no	दस्तावेजों का विवरण /Details of documents	प्रकाशन तिथि(दिन/माह/वर्ष) /Publication date	उद्धरित दस्तावेज का प्रासंगिक विवरण (पृष्ठ व अनुच्छेद संख्या) /Relevant description (page and paragraph no.) of cited document	अभिकथित आविष्कार के दावे /Relevant claims of cited document	अभिकथित आविष्कार के दावे /Claims of alleged invention
1	S A Joshi et al: "Fabrication and in-vivo evaluation of lipid nanocarriers based transdermal patch of colchicine", Journal of Drug Delivery Science and Technology, vol. 41, 2017, pages 444-453, DOI: 10.1016/j.jddst.2017.08.013	26/08/2017	the whole document		1-10
2	H P Singh et al: "Elastic liposomal formulation for sustained delivery of colchicine: in vitro characterization and in vivo evaluation of anti-gout activity", The AAPS journal, vol. 11, no. 1, 2009, pages 54-64, DOI: 10.1208/s12248-008-9078-8	01/03/2009	the whole document		1-10
3	B V Bonifacio et al: "Nanotechnology-based drug delivery systems and herbal medicines: a review", International Journal of Nanomedicine, vol. 9(1), 2014, pages 1-15, DOI: 10.2147/IJN.S52634	09/12/2013	abstract		1-10

ख. अधिनियम के तहत आवश्यकताओं पर विस्तृत टिप्पणियां /B. Detailed observations on the requirements under the Act:

(1).नवीनता / NOVELTY:

(I) ऊपर उद्धरित दस्तावेज के संदर्भ (1-10) में दिये गए प्रकटन के पूर्वानुमान को ध्यान में रखते हुए, निम्नलिखित कारणों से दावा(वों) (1-10) में नवीनता की कमी है /

Claim(s) (1-10) lack(s) novelty, being anticipated in view of disclosure in the document cited above under reference D1 for the following reasons:

The present application does not meet the requirements of section 2(1)(j) of the Patents Act because the subject-matter of claims 1-10 is not new within the meaning of section 13(1)(a) of the Patents Act.

D1 discloses (see the whole document) a formulation and evaluation of solid lipid nanoparticles (SLNs) based transdermal patch of colchicine. Preparation of colchicine loaded SLNs (C-SLNs) by ultrasonication method and optimization with respect to the concentration of lipid and surfactant are also elaborated in D1 (see paragraph "2.3. Preparation of colchicine-solid lipid nanoparticles(C-SLNs)" and Table 1). D1 also discloses an improvement in the bioavailability of the colchicine by incorporating it in SLNs based transdermal patch and to evaluate their in vivo anti-gout potential in rats by Monosodium urate induced subcutaneous air pouch model (see paragraph "3. Result and discussion").

Claims 1-10 is therefore not novel over D1.

(2). आविष्कारी कदम / INVENTIVE STEP:

(I) ऊपर उद्धरित दस्तावेज़(जों) के संदर्भ D1-D5 में स्पष्ट अध्यापन(नों) को ध्यान में रखते हुए, निम्नलिखित कारणों से दावा(वों) (1-10) में आविष्कारी कदम की कमी है

Claim(s) (1-10) lack(s) inventive step, being obvious in view of teaching (s) of cited document(s) above under reference D1-D5 for the following reasons:

Claims 1-10 of the alleged application does not involve an inventive step u/s 2(1)(ja) of the Patents Act as being obvious in view of the following prior art documents:

D1: S A Joshi et al: "Fabrication and in-vivo evaluation of lipid nanocarriers based transdermal patch of colchicine", Journal of Drug Delivery Science and Technology, vol. 41, 2017, pages 444-453, DOI: 10.1016/j.jddst.2017.08.013 (26/08/2017)

D2: WO 2012/176212 A4 (27/12/2012)

D3: H P Singh et al: "Elastic liposomal formulation for sustained delivery of colchicine: in vitro characterization and in vivo evaluation of anti-gout activity", The AAPS journal, vol. 11, no. 1, 2009, pages 54-64, DOI: 10.1208/s12248-008-9078-8 (01/03/2009)

D4: B V Bonifacio et al: "Nanotechnology-based drug delivery systems and herbal medicines: a review", International Journal of Nanomedicine, vol. 9(1), 2014, pages 1-15, DOI: 10.2147/IJN.S52634 (09/12/2013)

D5: WO 2013/166498 A1 (07/11/2013)

Since none of the claims are novel, there's no distinguishing technical feature(s) found which solve the technical problem posed in an inventive manner.

D2 discloses (see abstract; claims 1-3) a lipid nano carrier based nanogel formulation of an active ingredient and method of their preparation. The formulation is specifically useful for dermal delivery or topical application of drugs, which may be a hydrophilic drug including colchicine (see claim 5). D2 further describes (see abstract) a method of preparing lipid nano carrier based nanogel formulation of an active ingredient comprising the steps of: preparation of drug loaded vesicular lipid carrier dispersion, wherein the surface of vesicles of the lipid carrier contains a surfactant, probe sonicating the drug loaded vesicular lipid carrier dispersion of step (a.) to prepare a lipid nano carrier dispersion in nanometric size range, concentrating the lipid nano carrier dispersion in nanometric range by steps of subjecting the lipid nano carrier dispersion in nanometric size range of step (b.) either to (i) rotary evaporation, or (ii) freeze drying with or without a cryoprotectant, preparation of hydrophilic gel; and mixing of lipid nano carrier dispersion of step (c.) with hydrophilic gel of step (b) to form a lipid nano carrier based nanogel formulation.

D3 also discloses (see the whole document) elastic liposome based sustained release drug delivery system of colchicine. The skin penetration, skin deposition and in-vivo antigout potential is also studied (see Table II to Table IV). The results indicates that elastic liposomal system has greater penetration and deposition potential as compared to conventional drug delivery systems (see paragraph "RESULTS AND DISCUSSION"). D3 does not disclose nanostructured lipid carriers (NLCs) based transdermal patch of colchicine.

However, nanostructured lipid carrier based drug delivery systems are well-known to a person skilled in the art. For example, D4 have explored the potential applications of nanocarriers based drug delivery systems in order to

enhance the efficacy of herbal drugs (see abstract). D5 also discloses (see page 2, line 18-page 3, line 8; claims 1-20) liposomal nanoparticles for drug delivery, particularly mucus-penetrating liposomal nanoparticles wherein colchicine is listed as an active ingredient (see page 22, lines 17-20).

Therefore, a person working in the field of drug delivery systems applying common general knowledge or starting from either of D4/ D5 would motivate to prepare a nanostructured lipid carriers (NLCs) based transdermal patch of known drug colchicine (cf. D1 through D3) for the same therapeutic application (i.e., anti-gout activity) without exercising an inventive merit.

Consequently claims 1-10 do not satisfy section 2(1)(ja) of the Patents Act.

(3).पेटेंट अयोग्यता /NON PATENTABILITY:

(I) निम्नलिखित कारणों से धारा 3 के खंड (e) के प्रावधान के तहत दावा(वे) (1-10) सांविधिक रूप से पेटेंट योग्य नहीं हैं / Claim(s) (1-10) are statutorily non-patentable under the provision of clause (e) of Section 3 for the following reasons:

Claims 1-10 of the alleged application falls within the scope of such clause (e) of section 3 of the Patent Act, as it appears that the claimed pharmaceutical composition comprising nanostructured lipid carriers (NLCs) based transdermal patch of colchicine is a mere admixture with no evidence of synergism provided in the specification and its process for preparation thereof.

(4).प्रकटन की दक्षता /SUFFICIENCY OF DISCLOSURE:

(I) विनिर्देश पूर्णतया: व विशेषकर आविष्कार तथा इसके संचालन तथा विधि के निष्पादन के संबंध में विवरण नहीं देते हैं।
The complete specification does not fully and particularly describe the invention and its operation and the method by which it is to be performed in respect of:

The application does not sufficiently define the invention because the application does not disclose the invention in a manner that is sufficiently complete for it to be carried out by the skilled person. The amount of the active ingredient, i.e., colchicine, lipid and excipients in the form of nanostructured lipid carriers (NLCs) based transdermal patch are not disclosed in the claims which is a crucial factor in such drug delivery systems. The lipids are also broadly defined and specific solid lipid/ liquid lipid as claimed in dependent claims extend beyond what is actually tested in working examples. Furthermore, the application does not demonstrate anything unexpected such as synergy between the components of the claimed composition comprising nanostructured lipid carriers (NLCs) based transdermal patch of colchicine. The present claims therefore lack support and the application so lacks sufficiency of disclosure within the meaning of section 10(4) of the Patents Act.

(II) आविष्कार में उपयोग की गयी जैविक सामग्री के स्रोत व भौगोलिक उद्गम की सूचना.
Information of source and geographical origin of biological material used in the invention:

Source and geographical origin of the biological material, i.e., Colchicine, Castor oil should be disclosed in the complete specification u/s 10(4)(ii)(D) of the Patents Act.

(5).स्पष्टता एवं संक्षिप्तता /CLARITY AND CONCISENESS:

(I) दावा(वे) 9 के संबंध में स्पष्ट रूप से परीभाषित नहीं हैं.
Claim(s) 9 are not clearly worded in respect of:

Claim 9 refers to the expression "used for the treatment of gout" which recites intended therapeutic use of the claimed composition. This so called result-to-be-achieved type of definition renders the subject-matter claimed unclear.

(6).राष्ट्रीय जैव विविधता अधिनियम (एनबीए) का अनुमोदन आवश्यक है /National Biodiversity Act(NBA) Approval Required :

(I) Attention of the applicant is invited towards Section 6 of the Biodiversity Act 2002 which mandates that if biological material obtained from India is used in the application for Patent, then permission and other information for making application for patent should be obtained from the National Biodiversity Authority and details should be furnished in the application Form 1 column 9 (iii).

(7).अन्य आवश्यकताएँ /OTHERS REQUIREMENTS:

(I)

The expression "according to claim(s)" should be replaced with "as claimed in claim(s)" in dependent claims.

भाग – III: औपचारिक आवश्यकताएँ /PART-III: FORMAL REQUIREMENTS

आपत्तियां /Objections	टिप्पणी /Remarks
Statement & Under Taking (Form 3 Details)	(i) Details regarding application for patents which may be filed outside India from time to time for the same or substantially the same invention should be furnished within six months from the date of filing of the said application under clause (b) of sub section (1) of section 8 and rule 12(2) of the Patents Act and Rules. (ii) Details regarding the search and examination report including prosecutions till the grant or refusal of a patent, as referred under section 8(2) of the Patents Act in respect of same or substantially the same invention filed in all the major Patent Office's such as USPTO, EPO, JPO etc., along with appropriate English translation where applicable, should be submitted within a period of six months from the date of receipt of this communication as provided under rule 12(3) of the Patents Rules.
Permission from NBA	The Applicant is required to obtain permission from the National Biodiversity Authority u/s 6 of the Biodiversity Act because the Applicant has used biological materials such as Colchicine, Castor oil obtained from India.
Format of Specification (rule 13)	Abstract should commence with the title of the invention u/r 13(7)(a) of the Patents Rules.
Other Deficiencies	Indian patent application number should be duly mentioned in Form 3 and Form 5.

भाग-IV: रिकॉर्ड में दस्तावेज़ /PART-IV: DOCUMENTS ON RECORD

निम्नलिखित दस्तावेज़ों के आधार पर यह परीक्षण रिपोर्ट तैयार की गयी है

The examination report has been prepared based on the following documents:

कार्यसूची तिथि	कार्यसूची संख्या /Docket	
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THE PATENT OFFICE

/ Docket Date	फाइल नंबर / Docket Number	प्रविष्टि संख्या विवरण / Entry Number Description
26 Apr 2018	19333	OTHERS(NON CASH)
26 Apr 2018	19333	1-New Application For Patent With Provisional /Complete Specification
26 Apr 2018	19333	3-Statement & Undertaking - Form 3
26 Apr 2018	19333	2-Complete After Provisional Specification - Form 2 Check For No. OF Pages & Claims
26 Apr 2018	19333	12-Request For Early Publication - Form 9
26 Apr 2018	19333	5-Declaration As To Inventorship - Form 5
14 Oct 2020	58891	45-Form Of Authorisation Of Patent Agent - Form 26
14 Oct 2020	58895	18(iii)-Changing Name/Address/Nationality/Address For Service - Form 13
14 Oct 2020	58895	28(i)-Request For Examination After 18 months Publication - Form 18

नियंत्रक का नाम /Name of the Controller: [Dr. Santosh Kumar Samantaray](#)

नियंत्रक स्थान /Controller Location: [Kolkata](#)

टिप्पणी: परीक्षण रिपोर्ट का उत्तर दाखिल करने की अंतिम तिथि / Note: Last date for filing response to the Examination Report:
03/06/2021