Welcome DR. P. ARUNASREE Sign out

Controller General of Patents, Designs & Trade Marks
G.S.T. Road, Guindy, Chennai-600032
Tel No. (091)(044) 22502081-84 Fax No. 044 22502066
E-mail: chennai-patent@nic.in
Web Site: www.ipindia.gov.in

सत्यमेव जयते

INTELLECTUAL PROPERTY INDIA
PATENTS | DESIGNS | TRADE MARKS
GEOGRAPHICAL INDICATIONS

G.A.R.6
[See Rule 22(1)]
RECEIPT

Docket No 6396 **Date/Time 2022/01/24 15:15:30**

To
DR. P. ARUNASREE

UserId: arunasree

GNANLex Associates LLP 335, 3rd floor, V Mall, Asha Nagar, Near Saidham, Thakur Complex Kandivali East, Mumbai - 400101, Maharashtra, India.

CBR Detail:

Sr. No.	Ref. No./Application No.	App. Number	Amount Paid	C.B.R. No.	Form Name	Remarks
1	E-106/349/2022/CHE	202241003834	0	-----	FORM28	
2	202241003834	TEMP/E-1/4446/2022-CHE	1600	2790	FORM 1	ORAL COMPOSITION COMPRISING THERMOSTABLE PROBIOTICS FOR ORAL HEALTH

TransactionID	Payment Mode	Challan Identification Number	Amount Paid	Head of A/C No
N-0000912244	Online Bank Transfer	2401220010689	1600.00	1475001020000001

Total Amount : ₹ 1600
Amount in Words: Rupees One Thousand Six Hundred Only

Received from DR. P. ARUNASREE the sum of ₹ 1600 on account of Payment of fee for above mentioned Application/Forms.

* This is a computer generated receipt, hecnce no signature required.

Print

Home About Us Contact Us

FORM 1 **THE PATENTS ACT 1970** **(39 OF 1970)** **AND** **The Patents Rules, 2003** **APPLICATION FOR GRANT OF PATENT** **(**See section 7, 54 and 135 and sub-rule (I) of rule 20**)**	(FOR OFFICE USE ONLY) Application No: Filing Date: Amount of Fee Paid: CBR No: Signature:
1. APPLICANT'S REFERENCE / IDENTIFICATION NO. (AS ALLOTTED BY OFFICE):	

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

Ordinary (✓)		Convention ( )		PCT-NP ()	
Divisional ()	Patent of Addition()	Divisional ()	Patent of Addition ()	Divisional ()	Patent of Addition ()

3A. APPLICANT(S):

Sr. No.	**Name in Full**	**Nationality**	**Country of Residence**	**Address of the Applicant**	
1	**Triphase Pharmaceuticals Private Limited**	**Indian**	**India**	House No.	**"Galaxy", Plot No.30**
				Street	**1st Main Road, 3rd Phase, J.P. Nagar**
				City	**Bengaluru**
				State	**Karnataka**
				Country	**India**
				Pin code	**560078**
2	**JSS Dental College And Hospital, JSS Academy Of Higher Education & Research**	**Indian**	**India**	House No.	**Dept Of Pediatric & Preventive Dentistry, JSS Dental College & Hospital**
				Street	**JSS Academy Of Higher Education & Research, JSS Medical Institutions Campus, S. S. Nagar**
				City	**Mysore**
				State	**Karnataka**
				Country	**India**
				Pin code	**570015**

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

Natural Person ()	Other than Natural Person ()			
	Small Entity (✓)	Startup ()	Educational Institution ()	Others ()

4. INVENTOR(S) [Please tick (✓) at the appropriate category]

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

If "No", furnish the details of the inventor(s)

Sr. No.	Name in Full	Nationality	Country of Residence	Address of the Inventors	
1	**DESHMUKH, Seema**	**Indian**	**India**	House No.	**Dept Of Pediatric & Preventive Dentistry, JSS Dental College & Hospital**
				Street	**JSS Academy Of Higher Education & Research, JSS Medical Institutions Campus, S. S. Nagar**
				City	**Mysore**
				State	**Karnataka**
				Country	**India**
				Pin code	**570015**
2	**SHARIEFF, Irfanulla**	**Indian**	**India**	House No.	**"Galaxy", Plot No.30**
				Street	**1st Main Road, 3rd Phase, J.P. Nagar**
				City	**Bengaluru**
				State	**Karnataka**
				Country	**India**
				Pin code	**560078**
3	**PRAKASH, Abhilash**	**Indian**	**India**	House No.	**"Galaxy", Plot No.30**
				Street	**1st Main Road, 3rd Phase, J.P. Nagar**
				City	**Bengaluru**
				State	**Karnataka**
				Country	**India**
				Pin code	**560078**
4	**DESIRAJU, Shrilakshmi**	**Canadian**	**India**	House No.	**"Galaxy", Plot No.30**

				Street	**1st Main Road, 3rd Phase, J.P. Nagar**
				City	**Bengaluru**
				State	**Karnataka**
				Country	**India**
				Pin code	**560078**

5. TITLE OF THE INVENTION:

"ORAL COMPOSITION COMPRISING THERMOSTABLE PROBIOTICS FOR ORAL HEALTH"

6. AUTHORISED REGISTERED PATENT AGENT(S):	IN/PA No.	**IN/PA 509**
	Name	**Dr. Gopakumar G. Nair**
	Mobile No.	**09594052272**
	IN/PA No.	**IN/PA 998**
	Name	**Dr. P. Aruna Sree**
	IN/PA No.	**IN/PA 2338**
	Name	**Chirag Sunil Dighe**
	IN/PA No.	**IN/PA 2725**
	Name	**Sheela Pawar**
	IN/PA No.	**IN/PA 2761**
	Name	**Manish Chemburkar**
	IN/PA No.	**IN/PA 2917**
	Name	**Bina Dandekar**
	IN/PA No.	**IN/PA 3778**
	Name	**Mr. Mitesh Patil**
	IN/PA No.	**IN/PA 3565**
	Name	**Ms. Vanija Verma**
	IN/PA No.	**IN/PA 3226**
	Name	**Mr. Umeshkumar Ku**

7. ADDRESS FOR SERVICE OF APPLICANT IN INDIA	Name	**Gnanlex Associates LLP**
	Postal Address	**335, 3rd floor, V Mall, Asha Nagar, Near Saidham, Thakur Complex Kandivali East, Mumbai - 400101, Maharashtra, India.**
	Telephone No.	**91-22-40895454**
	Mobile No.	**09594052272**
	Fax No.	
	E-mail ID	**ipr@gnanlex.net gopanair@gnaipr.net**

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)
-	-	-	-	-	-

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 as allotted by the receiving office
-	-

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

Original (first) application number	Date of filing of Original (first) application
-	-

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

12. DECLARATIONS

(I) Declaration by the inventor(s)

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

I/We, the above named 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 12/01/22
(b) Signature(s)
(c) Inventor Name(s): Dr. Seema Deshmukh

(a) Date 12/01/2022
(b) Signature(s)
(c) Inventor Name(s): Sharieff, Irfanulla

(a) Date 12/01/2022
(b) Signature(s)
(c) Inventor Name(s): Prakash, Abhilash

(a) Date 12/01/2022
(b) Signature(s)
(c) Inventor Name(s): Desiraju, Shrilakshmi

(ii) Declaration by the applicant(s) in the convention country

(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/aremy/our assignee or legal representative.

(a) Date
(b) Signature(s)
(c) Name(s) of the signatory

(iii) Declaration by the applicant(s):

We, the applicant(s) hereby declare(s) that:-

☑ We are in possession of the above-mentioned invention.

☑ The Provisional specification relating to the invention is filed with this application.

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

☑ There is no lawful ground of objection to the grant of the Patent to us.

☑ 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_____ (DD/MM/YYYY) 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) Provisional specification (Total No. of sheets 18)

Item	Details	Fee	Remarks
~~Complete~~/provisional specification)#	No. of pages: 17	Rs. 1600/-	
No. of Claim(s)	No. of pages: 00 No. of claims: 00		
Abstract	No. of pages: 01		
Drawings	No. of pages: 00 No.of Drawings: 00		

#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) Statement and undertaking on Form 3;

(c) Online payment of official Fee **Rs. 1600/-**

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

Dated this 24th day of January, 2022

Dr. P. Aruna Sree
(Regn.No.: IN/PA 998)
Agent for the Applicant
Gnanlex Associates LLP

To,
The Controller of Patents
The Patent office, At Chennai.

FORM 2

THE PATENTS ACT, 1970

(39 of 1970)

AND

The Patents Rules, 2003

PROVISIONAL SPECIFICATION

(See section 10 and rule13)

1. TITLE OF THE INVENTION:

"ORAL COMPOSITION COMPRISING THERMOSTABLE PROBIOTICS FOR ORAL HEALTH"

2. APPLICANT:

(1) (a) NAME: **TRIPHASE PHARMACEUTICALS PRIVATE LIMITED**

(b) NATIONALITY: **Indian Registered Company**

(c) ADDRESS: "**Galaxy", Plot No.30, 1st Main Road, 3rd Phase, J.P. Nagar, Bengaluru-560078, Karnataka, India.**

(2) (a) NAME**: JSS DENTAL COLLEGE AND HOSPITAL, JSS ACADEMY OF HIGHER EDUCATION & RESEARCH**

(b) NATIONALITY: **Indian**

(c) ADDRESS: **Dept Of Pediatric & Preventive Dentistry, JSS Dental College & Hospital, JSS Academy Of Higher Education & Research, JSS Medical Institutions Campus, S S Nagar, Mysore-570015, Karnataka, India**.

3.PREAMBLE TO THE DESCRIPTION:

The following specification describes the present invention

TECHNICAL FIELD OF THE INVENTION:

The present invention relates to an oral composition comprising thermostable probiotic selected from *Lactobacillus sp.*, useful for inhibiting the growth and activity of harmful bacteria causing dental caries and for maintaining the oral health. The present invention also relates to a process for preparation of said oral composition.

BACKGROUND AND PRIOR ART OF THE INVENTION:

Dental caries is one of the most common diseases in the world – second only to the common cold. Dental caries can be prevented by maintenance of proper oral hygiene with the use of oral care products like toothpaste, toothbrush, mouthwashes and also including mucoadhesive patches and buccal films with antimicrobial and anti-cariogenic properties.

Oral care is the best way to deal with the harmful bacteria in the mouth. Bad bacteria are disease-causing and lead to an array of oral health conditions such as bad breath, gingivitis, periodontitis, cavities, and plaque build-up. The beneficial bacteria, like probiotics, aid in the digestion of foods, and protect the teeth and gums from bad bacteria, which can easily grow out of control.

The major causative organism responsible for dental caries is *Streptococcus mutans*. The level of *Streptococcus mutans* in the saliva is a reflection of the number of tooth sites that have been colonized as well as their proportion in dental plaque.

Streptococcus mutans plays a pivotal role in the development of caries. The bacterium converts fermentable sugars into organic acids and thus generates an acidic microenvironment. The organic acids are capable of demineralizing the dental enamel and thus bring about, or promote, the cariotic lesions. S. mutans is considered

to be necessary for the development of cariotic lesions. Salivary *Streptococcus mutans* levels reflect the number of tooth sites that have been colonized as well as their proportion in dental plaque.

Probiotic is a type of microorganism (such as *lactobacillus, Bifidobacterium*) which when consumed as a food or a dietary supplement, maintains or restores the beneficial bacteria of the digestive tract. The product containing live microorganisms to confer a health benefit to humans can be termed as a probiotic. These microorganisms/bacteria are strong against the harsh conditions of the stomach and surprisingly they can reach to the intestine lively in large numbers to impart their effect. The World Health Organization (WHO) and the Food Agriculture Organization (FAO) recognize the importance of these microorganisms/bacteria in maintaining a healthy digestive system and better immunity for improved overall health.

Probiotics have been used in combating various diseases such as gastro-intestinal infections, cancer prevention, constipation, irritable bowel syndrome, periodontal diseases and dental caries.

Usual form of giving probiotics is in the form of sachet which is taken with liquid to increase the gut bacteria. The balance between the beneficial and harmful gut bacteria plays a role during any disease condition. Like the gut, the mouth has its diverse bacterial community known as the oral microbiome.

The mechanisms of action of probiotics in the human body include normalisation of the microbiota, modulation of immune response and metabolic effects. Probiotics in the oral cavity have been used to replace cariogenic organisms like streptococci and lactobacillus species with strains of bacteria that are not cariogenic. Dental probiotics are similar to gut probiotics in that they use good bacteria to improve the health of the microbiome in the mouth. Oral probiotics are most effective when delivered and absorbed directly in the mouth via mucosal patches, oral films, lozenges, chewable

tablets. Such oral probiotic supplements deliver bacterial strains that are retained in the mouth so that they can colonize the surfaces in the mouth and form biofilms.

US6872565 discloses a product for inhibiting growth of dental caries bacteria, comprising *Limosilactobacillus reuteri* since the reuteri strain selected from the group consisting of *Limosilactobacillus reuteri* strain ATTC PTA-4965 and *Limosilactobacillus reuteri* strain ATTC PTA-4964, said strains having inhibitory activity against cariogenic bacteria in combination with good binding to oral mucins.

US8137952 discloses a *Lactobacillus* genus that has the ability to survive in high temperature environments and incorporated in food products for treating Coeliac disease. It also discloses two novel strains of *Lactobacillus* genus- *Lactiplantibacillus plantarum* LB3e and *Lactiplantibacillus plantarum* LB7c. The thermostable strains used in the prior art are freeze dried at - 80°C. Freeze drying is performed because the Lactobacillus strains cannot with stand high temperature, so the strains LB931, LB21, LB3e & L1A have been formulated using cryoprotectants.

US9155766 discloses a probiotic composition comprising a mixture of at least two oral health improving probiotic bacteria, including Streptococcus salivarius K12® (BLIS K12®) and Lacticaseibacillus paracasei Lpc-37 SD5275, formulated for oral administration.

WO2016051358 discloses food products comprising of thermostable strain of *Lactobacilli* prepared using Strainboost® technology which eliminates the need for cold storage, wherein the thermostable microorganism is selected from group comprising *Lactiplantibacillus plantarum* with ATCC SD No. 6863 and *Lactobacillus acidophilus* with ATCC SD No. 6864.

A research article titled, “Mucoadhesive wafers for buccal delivery of probiotic bacteria: Mechanical properties and enumeration” by Sabrina Barbosaet. al. discloses the development of wafers systems containing poloxamer 407, Carbopol 974 P, probiotic microorganisms *Bifidobacterium bifidum* BB12 for oral cavity administration. It discoses the application of probiotics to the oral cavity for preventing or countering gingivitis and periodontitis by various effects such as anti-inflammatory, anti-bacterial, adherence promotive and microbiota influencing effects in the oral cavity. Using the most concentrated formulation of BB12 ($1.63x10^{19}$ Cfu/ml) demonstrated more difficulties in freeze drying process. The probiotic wafers are prepared in cold conditions. The wafers could be stored only for 14 days with probiotic benefits. The viable count of BB12 in wafers declined within 0 to 21 days of storage which shows low stability. The storage temperature of wafers is also not disclosed.

EP3141242 discloses a mucoadhesive probiotic composition and corresponding dosage form, which can deliver an active substance within the oral cavity, especially an orodispersible tablet for delivering probiotic substance.

A research article titled “A postbiotic is not simply a dead probiotic” by Dr. Gabriel Vinderola discloses that a probiotic product, which is not kept in cold storage or cold chain and is kept at room temperature for long duration, an overage of 0.5 to 1 log order CFU is included or added to attain the expected viable cell count at the end of the shelf life.

The use of *Lactobacillus* strains to treat oral disorders is known. However, most of the probiotics are susceptible to environmental conditions and cannot survive in a harsh environment during manufacturing. Thus, there is a high possibility that the probiotics in the oral products are not viable or denatured before its use/application.

Moreover, Probiotic containing products need to be transported and stored effectively so as to maintain the viability of microorganisms/bacterias which have been incorporated in the products. A common method for storing and transporting the probiotic products is cold storage or using cold chain (2° C. to 8° C), which is highly expensive and complicated process.

Therefore, there remains an unmet need to provide an oral care composition which comprises temperature-stable probiotic strains that has the ability to withstand manufacturing processes, remain viable outside the cold chain, do not require refrigeration during transport and storage and meets the expected viable cell count at the end of the shelf life without overages during manufacturing.

Thus, the present inventors have exerted ingenuity in arriving at oral composition comprising thermostable probiotic selected from Lactobacillus sp. that are viable outside cold chain, thus resulting in cost saving for the supply chain. These oral compostions can be used as an effective adjuvant to daily oral hygiene maintenance routine. A recent study by Piqué, Berlanga, and Miñana-Galbis (2019) revealed that *L. rhamnosus GG* has the highest value of adhesion and inhibits Streptococcus by producing different antimicrobial components such as organic acid, hydrogen peroxide, carbon peroxide and diacetyl bacteriocins. The most used probiotics for oral applications are *L. rhamnosus, L. reuteri, L. paracasei, B. lactis, Streptococcus salivarius* etc in single or combinations. The prior art literature fails to provide application of thermostable probiotic in oral health care products.

OBJECT OF THE INVENTION:

In accordance with the above, it is an object of the present invention to provide a oral composition comprising at least one strain of thermostable probiotic bacteria selected from Lactobacillus sp., useful for inhibiting the growth and activity of harmful bacteria causing dental caries and for maintaining the oral health.

Another object of the present invention to provide a process for the preparation of said oral composition.

SUMMARY OF THE INVENTION:

In a preferred aspect, the present invention provides a oral composition comprising at least one strain of thermostable probiotic bacteria selected from Lactobacillus sp., useful for inhibiting the growth and activity of harmful bacteria causing dental caries and for maintaining the oral health.

In another aspect, the present invention provides a oral composition comprising at least one strain of thermostable probiotic bacteria selected from *Lactiplantibacillus plantarum, Lacticaseibacillus rhamnosus, Lactobacillus acidophilus, Limosilactobacillus reuteri, Lacticaseibacillus paracasei* and the like.

In another aspect, the present invention provides an oral composition comprising at least one strain of thermostable probiotic bacteria selected from *Lactiplantibacillus plantarum, Lacticaseibacillus rhamnosus, Lactobacillus acidophilus, Limosilactobacillus reuteri, Lacticaseibacillus paracasei,* which is effective in inhibiting *Streptococcus mutans* in the oral cavity.

In yet another aspect, the present invention provides an oral composition comprising at least one strain of thermostable probiotic bacteria selected from *Lactiplantibacillus plantarum, Lacticaseibacillus rhamnosus, Lactobacillus acidophilus, Limosilactobacillus reuteri, Lacticaseibacillus paracasei,* along with anti-cariogenic and anti-bacterial agents; wherein said composition helps in slow release of the active in the oral cavity.

In yet another aspect, the present invention provides an oral composition comprising at least one strain of thermostable probiotic bacteria selected from *Lactiplantibacillus plantarum, Lacticaseibacillus rhamnosus, Lactobacillus acidophilus, Limosilactobacillus reuteri, Lacticaseibacillus paracasei* remains viable outside the cold chain and eliminates the need for cold storage. Commercial probiotic products employ freeze dried organisms which require continuous cold storage for the viability of the culture. Commercially available probiotics are enteric coated before drying, so that they can be stored at different temperature based on geographical zones. The storage conditions varies with repect to each strains & the kind of cryoprotectant used for stability.

In another preferred aspect, the present invention provides an oral composition comprising a probiotic blend of thermostable Lactobacillus sp., selected from *Lactiplantibacillus plantarum* and *Lacticaseibacillus rhamnosus*, effective for inhibiting the growth and activity of *S. mutans* causing dental caries and for maintaining the oral health.

In another aspect, the present invention provides a process for preparation of said oral composition.

DETAILED DESCRPITION OF THE INVENTION

The invention will now be described in detail in connection with certain preferred and optional embodiments, so that various aspects thereof may be more fully understood and appreciated.

Source and Geographical origin of biological materials:

Lactiplantibacillus plantarum - Isolated from Food, Procurred from MTCC (deposited at MTCC by ATCC)

Lacticaseibacillus rhamnosus - Isolated from curd, Katpadi, Vellore, Tamil nadu,India

Lactobacillus acidophilus- Isolated from food Nauni, Solan, Himachal Pradesh, India

In a preferred embodiment, the present invention discloses an oral composition comprising at least one strain of thermostable probiotic bacteria selected from *Lactiplantibacillus plantarum, Lacticaseibacillus rhamnosus, Lactobacillus acidophilus, Limosilactobacillus reuteri, Lacticaseibacillus paracasei,* useful for inhibiting the growth and activity of S. mutans causing dental caries and for maintaining the oral health.

In yet another embodiment, the present invention discloses an oral composition comprising at least one strain of thermostable probiotic bacteria selected from *Lactiplantibacillus plantarum, Lacticaseibacillus rhamnosus, Lactobacillus acidophilus, Limosilactobacillus reuteri, Lacticaseibacillus paracasei,* along with anti-cariogenic and antimicrobial agents; wherein said composition helps in slow release of the active in the oral cavity.

Accordingly, the anti-cariogenic agents are selected from Sanguinarine, Apigenin, tt-farnesol, and Macelignan are some examples of promising natural anticariogenic substances.
Sodium fluoride, Stannous fluoride, Sodium mono-fluoro phosphate, Amine fluorides, Stannous hexafluorozirconate, casein phosphopeptide-amorphous calcium phosphate, Xylitol.; and the anti-bacterial agents are selected from
Antibiotics like – Amoxicillin, Amoxicillin clavulanic acid, Clindamycin, Azithromycin, Ciprofloxacin, Metronidazole, Gentamycin, Penicillin, Chlorhexedine Calcium hydroxide, Mixture if tetracycline acid detergent (MTAD), Iodine, Graphene oxide, Methacrylate, Sodium hypo chloride, Chitosan.

In yet another embodiment, the present invention discloses an oral composition comprising at least one strain of thermostable probiotic bacteria selected from *Lactiplantibacillus plantarum, Lacticaseibacillus rhamnosus, Lactobacillus*

acidophilus, Limosilactobacillus reuteri, Lacticaseibacillus paracasei, remains viable outside the cold chain and eliminates the need for cold storage, which is thus resulting in cost saving for the supply chain

In another preferred embodiment, the present invention discloses an oral composition comprising a probiotic blend of thermostable *Lactobacillus sp.*, selected from *Lactiplantibacillus plantarum* with ATCC SD No. 6863 and *Lacticaseibacillus rhamnosus* with ATCC SD No. 7115, effective for inhibiting the growth and activity of S. mutans causing dental caries and for maintaining the oral health.

In yet another embodiment, the present invention discloses an oral composition comprising *Lactiplantibacillus plantarum* with ATCC SD No. 6863 has genomic sequence set forth in SEQ ID No. KR340471.

In yet another embodiment, the present invention discloses an oral composition comprising *Lacticaseibacillus rhamnosus* with ATCC SD No. 7115 has genomic sequence set forth in SEQ ID No. MF682285.

The Probiotic dosing varies depending on the product and specific indication. No consensus exists about the minimum number of microorganisms that must be ingested to obtain a beneficial effect. Typically, a probiotic should contain several billion microorganisms to increase the likelihood of adequate dental colonization. For *Lactobacilli* dental colonization, typical doses used range from 0.1 Billion Cfu to 5 Billion Cfu colony-forming units per day.

In yet another embodiment, the present invention discloses an oral composition comprising *Lactiplantibacillus plantarum* with ATCC SD No. 6863 contains a total viable cell count of NLT 250 Billion cfu/gm.

In yet another embodiment, the present invention discloses an oral composition comprising *Lacticaseibacillus rhamnosus* with ATCC SD No. 7115 contains a total viable cell count of _ NLT 160 Billion cfu/gm.

In yet another embodiment, the present invention discloses an oral composition comprising a probiotic blend of Lactobacillus sp., selected from *Lactiplantibacillus plantarum* with ATCC SD No. 6863 and Lacticaseibacillus rhamnosus with ATCC SD No. 7115 contains a total viable cell count of 1 billion cfu/gm for a mucoadhesive patch inhibiting 98% of S. mutans in the mouth.

In another preferred embodiment, the present invention discloses an oral composition comprising viable colony forming units (CFU) of at least one strain of thermostable probiotics selected from *L. Plantarum* or *L. Rhamnosus*; wherein said strain is thermostable at a temperature range of ^{o}C and maintaining 100% viability of the bacteria.

In another embodiment, the present invention discloses an oral composition comprising viable colony forming units (CFU) of a probiotic blend of thermostable *Lactobacillus sp.*, selected from *Lactiplantibacillus plantarum* with ATCC SD No. 6863 and *Lacticaseibacillus rhamnosus* with ATCC SD No. 7115; wherein said strain is thermostable at a temperature range of 25^{o}C to 100^{o}C ^{o}C and maintaining 100% viability of the bacteria.

In another embodiment, the present invention discloses a process for preparation of said oral composition.

In yet another embodiment, the present invention discloses an oral composition comprising at least one strain of thermostable probiotic bacteria selected from *Lactobacillus sp.*, or an oral composition comprising probiotic blend of thermostable *Lactobacillus sp.*, selected from *Lactiplantibacillus plantarum* and *Lacticaseibacillus*

rhamnosus; wherein said compositions can be prepared in the form of mucoadhesive patches, gummies, oral disintegrating film (ODF), ointment, liquid drops, dentifrice, toothpaste, mouthwash, lozenges, chewable tablets, probiotic drinks, pills, powders or beverages.

In yet another embodiment, the present invention discloses an oral composition comprising viable colony forming units (CFU) of a probiotic blend of thermostable Lactobacillus sp., for which the expected viable cell count throughout the shelf life is attained outside the cold chain and eliminates the need for cold storage.

In another embodiment, the present invention discloses mucoadhesive patch form of drug delivery of oral composition which is more effective over other forms such as gummies, chewing gums, toothpaste, etc. The present mucoadhesive patch of oral composition provides sustained release in the area of interest and shows less compliance issues in younger children.

Examples: Following examples are given by way of illustration therefore should not be construed to limit the scope of the invention.

Example 1: Muco-adhesive patch:

Method of Preparation of Mucoadhesive Buccal patches:

Method of Formulation of cinnamon bark oil incorporated, probiotic blend [*L. plantarum* (TSP-Lp1) and *L. rhamnosus* (TSP-Lrh1)] incorporated and placebo Mucoadhesive patch. The mucoadhesive patches were optimized for various formulation ingredients before making the final batches of mucoadhesive patches.

Mucoadhesive patches were prepared using the solvent casting technique. All the materials used for the patch preparation are approved by the FDA and come under the category of GRAS (Generally regarded as safe). Carbopol 934P and

Hydroxypropyl methylcellulose (HPMC) K15LV were used as the mucoadhesive polymers and polyethylene glycol (PEG) 4000 was used as the plasticizer. Stevia was used as a sweetening agent.

Preparation of Mucoadhesive Buccal Patches:

The buccal patches composed of combinations of Carbopol 934P, Hydroxypropyl methylcellulose (HPMC) K15LV, containing cinnamon oil & probiotic blend of *Lactobacillus plantarum* TSP-Lp1 and *Lactobacillus rhamnosus* TSP-LRh1 were prepared using a 54-cm^2 petri dish by solvent casting technique. Backing membrane was casted by pouring aqueous solution on aluminium foil in petri dishes at 42°C and left for 10h. Phosphate buffer saline, pH 6.8, was used as solvent in the casting method.

1.5 L of the cinnamon bark oil (20 µL per patch) and 10 mg of the probiotic blend [5 billion of *L. plantarum* (TSP-Lp1) and 5 billion of *L. rhamnosus* (TSP-Lrh1)] was required for a batch of 75 patches. Mucoadhesive patches were cut in 1 × 1 cm size and evaluated for thickness uniformity, weight uniformity, and pH. The matrices were prepared by pouring 40 ml of the homogeneous solutions on the aluminum foil backing membrane. Then, these buccal patches were dried at 42°C in an incubator After 24 h, the dried patches were removed from the petri dishes and kept in desiccators until use. Patches were placed on the palatal slope. The buccal cavity is easily accessible for self-medication, and hence it is safe and well accepted by patients, since buccal patches can be very easily administered and even removed from the application site, terminating the input of drug whenever desired. Moreover, buccal patches provide more flexibility than other drug deliveries.

A mucoadhesive patch incorporated with anti-cariogenic and antimicrobial agents may help in slowly releasing the drug in the oral cavity where there is a constant circulation of the drug in the oral cavity through saliva and hence it has a potential to be used as an alternative to mouthwash especially in the pediatric age group.

The point about overages to be exemplified here for example.

Experiment to show for a particular dosage form there is loss in potency of the probiotic culture from X to Y at a temp of 25^{o}C- marketed strain, TSP strain or an experiment to show label claim potency is not met for marketed strain without refrigeration.

Example 2: Chewing gum

Ingredients:

1. Gum base
2. Sweetening agents
3. Humectants
4. Softners
5. Preservative
6. Flavoring agent
7. ***Lactobacillus spp*** - The quantity will vary based on the viable count of *Lactobacillus spp* and label claim required per Chewing gum

Method of preparation:

1. Heat the ingredients:

- Add all the ingredients except sweetening agent in the top part of a double boiler. Placing the double boiler on the stove on medium high flame. Heat the mixture at 100°C & stir until it becomes warm, soft and sticky.

2. Pour the gum base into the well:

- Keep aside a tablespoon of sweetening agent and pour the remaining on a cutting board or clean work surface.
- When the gum temperature is between 70°C - 75°C, add the probiotic (*Lactobacillus spp*) as per the requirement and mix it uniformly for 5 min based on batch size.
  (Ex: If we need 500 million cfu/chewing gum,we need to calculate accordingly based on gummy batch size & Initial viable count of Lactobacillus spp (Ex:150 x109 Cfu/g)

- Carefully pour the melted gum base from the double boiler into the sweetening agent well.

4. Make bubble gum dough:

- Knead the mixture from step 1 and the sweetening agent together. Keep kneading the mixture (sweetening agent into the gum base) until the base gets sticky, then add more sweetening agent. Knead for at least 15 minutes, until the dough is soft and pliable and no longer sticky.
- If the dough is not kneaded enough, the gum will tend to fall apart.
- The dough should be smooth and stiff at the end.

5. Roll out the dough:

- Roll the dough using rolling pin till it becomes flat
- Cut it in neat square based on weight required (1.0 to 2.0 gm per chewing gum or as per label claim)
- Dust the gum pieces with powdered sugar to keep them from sticking to each other
- Wrap the gum pieces in small square pieces of parchment paper

Example 3: Toothpaste

Probiotic Strains: *Lactobacillus plantarum* TSp-Lp1 & *Lactobacillus rhamnosus* TSP-LRh1

1. **Essential Ingredients**

Water
Anticaries agent
Polishing agent
Stain remover
Surfactant, or foaming agent
Thickenining agent
Preservative
Antimicrobial agent
Flavouring agent

2. **Optional Ingredients**

Emusifier
Mild abrasives
Antifreeze or wetting agent
stabilizing agent
Sweetening agent
Anti- inflammatory agent

Example 4: Mouth wash

Ingredients

Water
Softners
Emulsifier, surfactants
Anticaries agent
Preservatives
Sweetening agent
Whitening agent
Antimicrobial, anti-inflammatory agent
Flavouring agent
Probiotic Strains: Lactobacillus plantarum TSp-Lp1 & Lactobacillus rhamnosus TSP-LRh1

Example 5: Clinical Study:

The temperature-stable probiotic strains, of *Lactiplantibacillus plantarum* (TSP-Lpl) & *Lacticaseibacillus rhamnosus* (TSP-) have the ability to withstand harsh manufacturing processes, especially required during making Food /Beverage and in the Pharma industries. Most of the probiotics currently available in the market cannot survive a harsh environment observed during manufacturing and acidic environment of the stomach. A study was conducted to evaluate the inhibitory activity of the lactobacillus strains individually and in combination to understand the inhibition against *S. mutans. Cinnamomum zeylanicum Blume* (cinnamon) is the potential herbal antimicrobial agent and now it has been replaced by probiotics.

It was a double blinded placebo-controlled study with n=60. They were randomly allotted into three groups- Group A-Cinnamon patch, Group B- Probiotic patch and Group C-Control patch (placebo) with n=20 in each group. In the first phase MIC of Cinnamon bark oil was determined against S. mutans followed by formulation of Cinnamon and Probiotic patches. After a washout period of 2 weeks and collection of baseline saliva samples, these patches were tested on the subjects from respective groups for 14 days with twice a day placement protocol. On the 15th day saliva samples were collected and cultured, cfu/ml of saliva of S. mutans for each subject was recorded and compared to baseline samples.

It is observed from the above study that the probiotic patch comprising individual strain of lactobacillus and blend of probiotics exhibits enhanced inhibition of S. mutans as that of Cinnamon patch.

Dated this 24th day of January, 2022

Dr. P. Aruna Sree
(Regn.No.: IN/PA 998)
Agent for the Applicant
Gnanlex Associates LLP

ABSTRACT

ORAL COMPOSITION COMPRISING THERMOSTABLE PROBIOTICS FOR ORAL HEALTH

The invention disclosed herein is an oral composition comprising thermostable probiotic selected from Lactobacillus sp., useful for inhibiting the growth and activity of harmful bacteria causing dental caries and for maintaining the oral health. The invention also disclosed herein is a process for preparation of said composition.

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) **TRIPHASE PHARMACEUTICALS PRIVATE LIMITED,** Indian Registered Company, having address as "Galaxy", Plot No.30, 1st Main Road, 3rd Phase, J.P. Nagar, Bengaluru-560078, Karnataka, India (2) **JSS DENTAL COLLEGE AND HOSPITAL, JSS ACADEMY OF HIGHER EDUCATION & RESEARCH,** Indian Nationality, having address as Dept Of Pediatric & Preventive Dentistry, JSS Dental College & Hospital, JSS Academy Of Higher Education & Research, JSS Medical Institutions Campus, S S Nagar, Mysore-570015, Karnataka, India, hereby declare:
2. Name, address and nationality of the joint applicant	(i) that We have not made any application for the same/substantially the same invention outside India Or (ii) that We who have made this application No. _____ dated **24th January, 2022** alone made for the same/substantially same invention, application(s) for patent in other countries, the particulars of which are given below:

Name of the Country	Date of Application	Application No./ Publication No.	Status of the Application	Date of Publication	Date of Grant
-	-	-	-	-	-

3. Name and address of assignee	(iii) that the rights in the application (s) has / have been assigned to **NA** that We undertake that upto the date of grant of the patent, by the Controller, 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 24th day of January, 2022**
4. To be signed by the applicant or his authorized registered patent agent	
5. Name of the natural person who has signed	**Dr. P. Aruna Sree** **(Regn.No.: IN/PA 998)** **Agent for the Applicant** **Gnanlex Associates LLP**
	To, **The Controller of Patents,** **The Patent Office,** At Chennai.

FORM 28
THE PATENTS ACT, 1970
(39 of 1970)
AND
The Patents Rules, 2003
TO BE SUBMITTED BY A SMALL ENTITY /STARTUP/EDUCATIONAL INSTITUTION
[See rules 2 (fa), 2(fb), 2(ca) and 7]

1.	Insert name, address and nationality	We, (1) **TRIPHASE PHARMACEUTICALS PRIVATE LIMITED,** Indian Registered Company, having address as "Galaxy", Plot No.30, 1st Main Road, 3rd Phase, J.P. Nagar, Bengaluru-560078, Karnataka, India (2) **JSS DENTAL COLLEGE AND HOSPITAL, JSS ACADEMY OF HIGHER EDUCATION & RESEARCH,** Indian Nationality, having address as Dept Of Pediatric & Preventive Dentistry, JSS Dental College & Hospital, JSS Academy Of Higher Education & Research, JSS Medical Institutions Campus, S S Nagar, Mysore-570015, Karnataka, India, in respect of the Provisional Patent Application No._____ filed on **24th January, 2022** hereby declare that ~~I/~~we ~~am/~~are **a small entity in accordance with rule 2(fa)** ~~or a startup in accordance with rule 2(fb) or an educational institution in accordance with rule 2(ca)~~ and submit the following document(s) as proof:
2.	Documents to be submitted	
	i. For claiming the status of a small entity:	
	A. For an Indian applicant: Evidence of registration under the Micro, Small and Medium Enterprises Act, 2006 (27 of 2006).	
	B. In case of a foreign entity: Any other document.	
	ii. For claiming the status of a startup	
	A. For an Indian applicant: Any document as evidence of eligibility, as defined in rule 2(fb).	
	B. In case of a foreign entity: Any other document.	
	iii For claiming the status of an educational institution	
	A. For an Indian applicant: Any document as evidence of eligibility, as defined in rule 2(ca).	
	B. In case of a foreign educational institution: Any other document.	
3.	To be signed by the applicant(s) / patentee (s) / authorised registered patent agent.	The information provided herein is correct to the best of my/our knowledge and belief. **Dated this 24th day of January, 2022** **Signature:**  **Name: Dr. P. Aruna Sree** **Designation: (Regn.No.: IN/PA 998)** **Agent for the Applicant** **Gnanlex Associates LLP** To The Controller of Patents, The Patent Office, at Chennai.
4.	Name of the natural person who has signed. Designation and official seal, if any, of the person who has signed.	
Enclosures:		MSME Certificate

भारत सरकार
Govt. of India
सूक्ष्म,लघु और मध्यम उद्यम मंत्रालय
MINISTRY OF MICRO, SMALL & MEDIUM ENTERPRISES

सूक्ष्म,लघु और मध्यम उद्यम
MICRO, SMALL & MEDIUM ENTERPRISES

उद्योग आधार Udyog Aadhaar

E

Type of Enterprise	Micro	Small	Medium
Manufacturing	A	B	C
Services	D	E	F
UAN	KR22E0004850		

Udyog Aadhaar Registration Certificate

Udyog Aadhaar Number: KR22E0004850

Name of Enterprise: TRIPHASE PHARMACEUTICALS PRIVATE LIMITED

Location of Plant Details

SN	Flat/Door/Block No.	Name of Premises/Building Village	Road/Street/ Lane	Area/Locality	City	Pin	State	District
1	Site No Special 3	Property No 482	KSSIDC Industrial Area	Kasaba Hobli	Hebbal	570016	KARNATAKA	MYSURU

Official Address of Enterprise: TRIPHASE PHARMACEUTICALS PVT LTD SITE NO SPECIAL 3, PROPERTY NO 482, KSSIDC INDUSTRIAL AREA, KASABA HOBLI, HEBBAL, MYSORE, KARNATAKA, INDIA PIN CODE :- 570016

District: MYSURU State: KARNATAKA PIN: 570016

Mobile No: 9731742239 Email: abhilashp@triphasepharma.com

Date of commencement: 01/06/2006

Major Activity: SERVICES

Enterprise Type: Small

Previous Registration details-if any: ,,

National Industry Classification Code

SN	NIC 2 Digit	NIC 4 Digit	NIC 5 Digit Code	Activity Type
1	21 - Manufacture of pharmaceuticals, medicinal chemical and botanical products	2100 - Manufacture of pharmaceuticals, medicinal chemical and botanical products	21001 - Manufacture of medicinal substances used in the manufacture of pharmaceuticals: antibiotics, endocrine products, basic vitamins; opium derivatives; sulpha drugs; serums and plasmas; salicylic acid, its salts and esters; glycosides and vegetable alkaloids; chemically pure suger etc.	Manufacturing

Acknowledgement Date of Filing: 02/05/2018 Date of Printing: 02/05/2018

Disclaimer: This is computer generated statement, no signature required.
Printed from udyogaadhaar.gov.in

MyMsme Mobile App (Beta Version) is available now for download. https://play.google.com/store/apps/details?id=msme.mymsme