



*Target Institute of Medical
Education & Research*

Corporate office :

A-402 A/B/C, Jaswanti Allied Business Centre,
Ramchandra Lane Extension, Kachpada,
Off Link Road, Malad West, Mumbai 400064
Phone : 022-28822252 / 022 32287239

Registered office :

205/B Blue Diamond Soc, L M Road,
Dahisar West, Mumbai 400068

To,
Dr. Shailesh Deshpande
Lecturer In Kayachikitsa
PDEA College Of Ayurveda & Research Center
Sector 25, Pradhikaran, Nigadi
Pune 28

Date : 5th Feb 2018

Subject : Budget for conducting Clinical Study on Ayurderme Capsules (Psoriasis)

Dear Dr. Shailesh Deshpande,

With regards to our discussions and further submission of documents for conducting clinical study on Ayurderme Capsules under the Title: "An Open Label, Single Arm, Multi-center, Prospective, Clinical Study to Evaluate Efficacy and Safety of WEL/PSO-01 in patients suffering from Chronic Plaque Psoriasis" we wish to submit the budget for the same below.

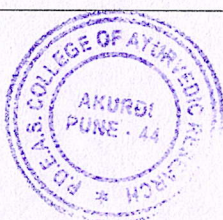
In this study we wish to have 10 completers. The below budget is submitted accordingly.

Sr No	Budget Head	Amount
1.	Ethics Committee Fees	15000/-
2.	Investigators Fees	10000/-
3.	Coinvestigator Fees	10000/-
4.	Research Associate/ coordinator Fees	10000/-
5.	Lab Charges*	At actual
6.	Institutional Charges	15000/-
7.	Department Development Fund	15000/-
8.	Total	75000/- Plus Lab Charges at Actual

Amount in words : Rs. Seventy Five Thousand Only Plus Lab Charges

*Lab Charges attached below.

We request you to kindly process the study at the earliest.





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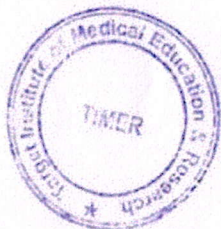
205/B Blue Diamond Soc, L M Road,
Dahisar West, Mumbai 400068

For any further details required in this regards please let us know.

Many thanks,

For,

Target Institute of Medical Education and Research,
Mumbai.



Investigation	No of times
CBC, ESR, Hb%	2
BSL-Fasting	1
Liver Function Tests (LFT): [SGOT, SGPT, Sr. Bilirubin Sr. Alkaline Phosphatase, Proteins total]	2
Renal Function Tests (RFT): [Sr. creatinine, BUN]	2
Lipid Profile: [Total sr. cholesterol, sr. triglycerides, LDL, HDL]	2
HIV I & II	1
Urine Routine & Microscopic	2
UPT	When Required



Date- 12 Feb 2018

To,
The Member Secretary
Institutional Review Board/ Institutional Ethics Committee
College of Ayurved & Research Centre,

Nigdi, Pune.

Ref. – “An open label, Single arm, Multi-centre, Prospective, Clinical Study to Evaluate Efficacy, & Safety of WEL/PSO-01 in patients suffering from Chronic Plaque Psoriasis.”

Protocol No. WLX/PSO-01, Version 1.0, Dated 09th Dec 2017.

Subject- Documents for Ethics Committee Submission & Approval

Respected Sir/ Madam,

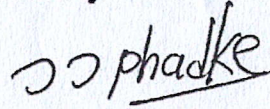
With reference to above mention Study please find enclosed Documents for Submission & approval.

Sr. No.	Documents	Version No.	No. of copies
1.	Clinical Study Protocol	Version 1.0, Dated 09 th Dec 2017.	1
2	Case Report form	Version 1.0, Dated 09 th Dec 2017.	1
3	Investigator Brochure	Version 1.0, Dated 09 th Dec 2017.	1
4	Inform Consent Document (Marathi)	Version 1.0, Dated 09 th Dec 2017.	1
5	Inform Consent Document (Hindi)	Version 1.0, Dated 09 th Dec 2017.	1
6	Inform Consent Document (English)	Version 1.0, Dated 09 th Dec 2017.	1
7	SAE Form	Version 1.0, Dated 09 th Dec 2017.	1
8	Prakruti Evaluation Form	Version 1.0, Dated 09 th Dec 2017.	1
9	Investigator Undertaken Form	Version 1.0, Dated 09 th Dec 2017.	1

Dr. Shailesh Deshpande


(Investigator)

Dr. Jayant Phadke


(Co-Investigator)



DATE: 24-Jan-2018

To,
Dr. Shailesh Deshpande
PDEA College of Ayurveda and Sterling Multi-specialty Hospital,
Pradhikaran Akurdi, Nigadi, Pune

**Ref: " An Open Label, Single Arm, Multi-center, Prospective, Clinical Study to Evaluate
Efficacy and Safety of WEL/PSO-01 in patients suffering from Chronic Plaque Psoriasis."**

Protocol no: WLX/PSO- 01, Version 1.0, Dated 09th Dec 2017

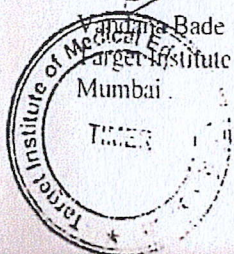
Sub.: Documents for Ethics Committee Submission and Approval

Dear Sir,

With reference to above mentioned study please find enclosed documents for submission and approval.

Sr. No	Document	Version No. & Date	No. Of Copies
1	Clinical Study Protocol	Version 1.0, Dated 09th Dec 2017	1
2	Case Report Form	Version 1.0, Dated 09th Dec 2017	1
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8	Prakruti Evaluation Form	Version 1.0, Dated 09th Dec 2017	1
9	Investigator Undertaken Form	Version 1.0, Dated 09th Dec 2017	1
10	Approval Pages(Clinical Study Protocol, SAE, CRF, Investigator Undertaken) ICF, Prakruti Evaluation)	Version 1.0, Dated 09th Dec 2017	1

Thanks and Regards,



Vandana Bade
Target Institute of Medical Education and Research,
Mumbai.



Clinical Study Protocol

Protocol No.: WLX/PSO-01, Version 1.0, Dated 09th Dec 2017

An Open Label, Single Arm, Multi-center, Prospective, Clinical Study to Evaluate Efficacy and Safety of WEL/PSO-01 in patients suffering from Chronic Plaque Psoriasis.

Protocol No. WLX/PSO- 01, Version 1.0, Dated 09th Dec 2017

The confidential information in the following document is provided to you as an investigator, co-ordinator and /or applicable institutional review board /ethics committee. By accepting this document, you agree that the information contained herein shall not be disclosed to others, without written authorization from Target Institute of Medical Education and Research (TIMER) and Sponsor Welex Laboratories Pvt. Ltd. except to the extent necessary to obtain informed consent from those persons to whom the study medications shall be administered or for regulatory purposes when asked by authorized regulatory personnel.



INVESTIGATOR STATEMENT

An Open Label, Single Arm, Multi-center, Prospective, Clinical Study to Evaluate Efficacy and Safety of WEL/PSO- 01 in patients suffering from Chronic Plaque Psoriasis.

Protocol No. WLX/PSO-01, Version 1.0, Dated 09th Dec 2017

We/I, the undersigned have read and understood this protocol and hereby agree to conduct the study in accordance with this protocol and to comply with all obligations of investigators and all pertinent requirements of the GCP guidelines laid down for ASU drugs.

We/I also consent to inform the Contract Research Organization (Target Institute of Medical Education and Research), Sponsor Welex Laboratories Pvt. Ltd., and concerned Ethics Committee of any serious adverse events and also to inform the Ethics Committee about the initiation and completion of the study.

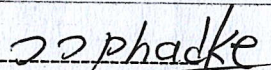
Site no

Site Name:

Address and Contact No:


Investigator

Sign and Date


Co-investigator

Sign and Date



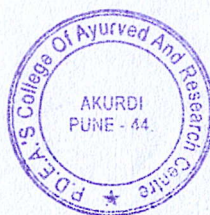
Clinical Study Protocol

Protocol No.: WLX/PSO-01, Version 1.0, Dated 09th Dec 2017

An Open Label, Single Arm, Multi-center, Prospective, Clinical Study to Evaluate Efficacy and Safety of WEL/PSO-01 in patients suffering from Chronic Plaque Psoriasis.

Protocol No. WLX/PSO- 01, Version 1.0, Dated 09th Dec 2017

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CLINICAL STUDY REPORT

Version: 1.0, Dated: 20th Apr 2019

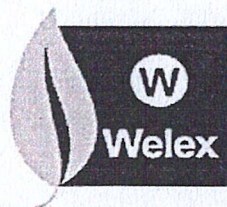
“An Open Label, Single Arm, Multi-center, Prospective, Clinical Study to Evaluate Efficacy and Safety of WEL/PSO-01 in patients suffering from Chronic Plaque Psoriasis.”

Protocol No.: WLX/PSO- 01, Version 1.0, Dated 09th Dec 2017

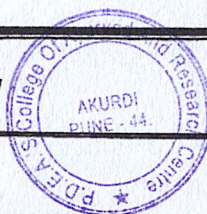
CTRI Registration Number: CTRI/2018/03/012615

Registered on 16/03/2018

Sponsor



**Welex Laboratories Pvt Ltd
1002, Marathon Innova Nextgen,
Off Ganpatrao Kadam Marg, Lower Parel,
Mumbai -400013**



To,

The Member Secretary
Institutional Ethics Committee
College of Ayurved & Research Centre,
Nigdi, Pune.

Date: 15 Oct 2018

Subject: Notification of Status – Psoriasis Clinical Study.

Reference: Clinical Study Protocol No.- WLX/PSO 01 /, Version 1.0, DATED ON 09 DEC 2017.

CTRI No. CTRI/2018/03/012615.

Respected Madam/Sir,

Herewith I am submitting you updated status report of Psoriasis Clinical study.

Duration- Jul-Sep 2018

Sr. No.	Details	Jul 2018	Aug 2018	Sep 2018
1	Total Screened	02	04	01
2	Screen Failure	00	00	00
3	Total Enrolled	02	03	01
4	Drop Out	01	00	01
5	Completer	00	03	00
6	Withdrew Consent	00	00	00
7	Total SAEs reported	00	00	00
8	Total AEs reported	00	01	00
9	ADR	00	00	00
10	Protocol Deviation	00	00	00
11	Protocol Violation	00	00	00

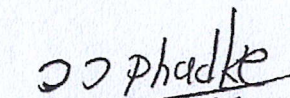
Reason for drop out-lost to follow up

-Thanks and Regards,



Dr. Shailesh Deshpande.

(Principal investigator)


Dr. Jayant Phadake

(Co-Investigator)



Pune District Education Association's
AYURVED RUGNALAYA & STERLING MULTISPECIALITY HOSPITAL
SECTOR NO.27,NIGDI,PUNE-44 GST NO:27AAATP1234H1ZS PH.NO.(020)27659460

Receipt

Receipt No :- 722

Receipt Date :- 20/06/2020

Received with thanks from

M/s :- **AYURVED RUGNALYA** * * * * *

the sum of Rupees :-30,000.00 In words :- RUPEES THIRTY THOUSAND ONLY

by Cheque no :- 000070

Dated :- 10/06/2020

as per particulars CLINICAL TRIAL FOR PROTEIN BY MPREX HEALTHCARE

Subject to realisation of cheque

FOR AYURVED RUGNALAYA & STERLING MULTISPECIALITY HOSPITAL

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POST AUNDH CAMP,PUNE-411027,MAHARASHTRA
RTGS / NEFT IFSC : HDFC0002524

10062020

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30,000/-

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Authorised Signatories

Please sign above / कृपया यहाँ हस्ताक्षर करें



College of Ayurved And Research Centre

Akordi, Pune - 411 044

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Assessment of the efficacy and safety of protein Supplement with micronutrient fortification (NRL/2019/5PNV) to promote health and wellbeing in healthy adults: Randomized controlled clinical trial

Priya Khare^{1*}, Omkar Kulkarni², Anuj Agarwal³, Gayatri Ganu⁴, Medha Joshi⁵, Manjit Sisode⁶

¹ Assistant Manager, Research and Development (Healthcare), Netsurf Research Labs Pvt Ltd, Baner, Pune, Maharashtra, India

^{2,3} Senior Manager, Research and Development (Healthcare), Netsurf Research Labs Pvt Ltd, Baner, Pune Maharashtra, India

⁴ Director, Clinical Research, Mprex Healthcare, Nisarg Plaza, Bhumkar Nagar, Wakad, Pune, Maharashtra, India

⁵ Professor, Pune District Education Association, Pune College Of Ayurveda & Sterling Hospital Research Center, Pradhikaran, Nigdi, Pune, Maharashtra, India

⁶ Director, Janseva multispecialty hospital, Old Agra Rd, Deopur, Dhule, Maharashtra, India

Abstract

Proteins are an essential component of the diet. As a source of good protein supplement for both male and female, Netsurf communication Pvt. Ltd. has developed NRL/2019/5PNV protein supplement with micronutrient fortification to help to manage health and quality of life. The current research depicts the efficacy and safety of the NRL/2019/5PNV. It is found to be safe and effective in promoting health and wellbeing in healthy adults. It improved skeletal muscle % and reduction in body fat %. There was increased physical endurance indicated as VO₂ max. NRL/2019/5PNV was found in improving energy levels in subjects along with improved digestive behavior. There was improved glycemic control and reduction in total cholesterol levels in NRL/2019/5PNV treated group. The blend of whey, soy, rice and peas protein with vitamin, micro minerals and rejuvenating herbal extracts like *Withania somnifera* and *Aloe vera* is definitely providing better assimilation and efficacy

Keywords: protein supplement, vo2 max, energy level, whey, soya, *Withania somnifera*, *Aloe vera*

1. Introduction

Proteins are an essential component of the diet needed for the survival of animals and humans. Nutritional quality of a food depends on protein content, digestion, absorption, and utilization of proteins. Amino acids availability depends on protein sources, processing treatments, and interaction with other components of the diet [1].

Source of proteins in human diet are mainly animal proteins (e.g. egg, milk, meat and fish) and plant proteins (e.g. pulses, cereals, nuts, beans and soy products). Animal proteins have high biological value than vegetable proteins as per amino acid composition and are more biologically complete. However two plant proteins such as legumes and grains or legumes and nuts/ seeds can be combined to formulate a complete protein from two incomplete proteins. There is gaining momentum to a fact that animal proteins are possessing concerns to many vegetarians and towards digestibility difficulties as well [2].

Legumes include peas, beans, lentils, peanuts etc. can be a good source of protein. Soybeans have captured more interest of researchers because of their concentrated source of isoflavones. It is being backed up by research that isoflavones reduce the risk of cancer, heart disease, and osteoporosis [3, 4]. Soy protein is thought by many researchers as almost equivalent to animal sources in protein quality [5]. According to a study, soy protein has beneficial effects in prevention of coronary heart disease, hypolipidemic effects [6]. Being rich source of isoflavone, soy protein help in improving bone health [7], menopausal symptoms [8] and preventing breast and prostate cancers [9]. Soy protein formulas are found suitable for feeding infants

who exhibit lactose intolerance or have lactase deficiency [10].

According to U.S. Food and Drug Administration, the term "dietary supplement" defines any product that supplements the diet containing any one or more of a vitamin, mineral, herb, botanical, amino acid to increase the total dietary intake of added contents [11, 12]. Plant-based supplements are rich in fiber, beta carotene, vitamin K and C, folate, magnesium, and potassium which improve dietary health index [13, 14]. There is great need of supplementing on Vitamin B12. Its deficiency leads to neurological and cognitive health weakening [15]. Vitamin B12 is suggested to be neuroprotective, particularly for memory performance [16-18].

As per many studies, supplementation with vitamin C reduces the duration and severity of common cold symptoms in adults [21, 22]. When used in combination with zinc, vitamin C supplementation can relieve symptoms such as rhinorrhea in common cold [23, 24]. According to the study, vitamin D supplements can protect against respiratory tract infections and reduce the risk of acute respiratory illness and influenza [25]. Studies has shown an excellent rationale to combine vitamins C and D with zinc to support immune functions and help minimize the risk of respiratory infection [26]. Micronutrients have proved helpful in combating the detrimental health effects of prolonged contact with environmental factors that act as vehicles for pollutants [27]. It is a proven fact that plant-based proteins are presented as lower in calories and fat than animal proteins and higher in fiber and essential nutrients. Plant-based pea proteins can help gain muscle mass, reduce hunger cravings. Its high

micronutrient profile helps reduce postmenopausal symptoms. Pea's protein is easily digested and leads to less gastric distress than animal based source.

Protein and fiber rich diet as per study was demonstrated to support successful weight-loss [28]. High-protein diets improve satiety and appetite control thereby providing an excellent way to control and reduce body weight [29]. Hunger and satiation define appetite pattern [30]. From a credible study it was hypothesized that hormones improvise hunger and satiety response such as insulin, glucagon, pancreatic polypeptide (PP) and amylin from pancreas, leptin and adiponectin from adipose tissue and ghrelin, glucagon-like peptide 1 and 2 (GLP-1, GLP-2) from intestine; and dopamine, neuropeptide Y, growth hormone releasing peptide (GHRP) from hypothalamus [31-32]. Orexigenic hormones or peptides promote appetite and anorexigenic work antagonistically, by suppressing appetite. The sensory exposure to food (e.g., sight, smell, taste) has been shown to improvise appetite [33].

High protein diets have been shown to be an effective weight-loss strategy by improving the pancreatic response to reduce hunger [34]. Proteins produce greater satiety than carbohydrates and fats. It increases energy expenditure [35]. Many researches back up the fact that protein diet gives postprandial appetite suppression and subsequent reduction in energy intake [36].

Omega-3 fatty acid, docosahexaenoic acid (DHA), is essential for normal brain function. It is a key component to support brain and eye function throughout life [37, 38]. It is also an important component of tissues of cardiovascular system. The American Heart Association and USDA Dietary Guidelines recommend Omega-3 fats as good for cardiovascular health [39].

By taking in to consideration the pressing need of good protein supplement for both male and female, Netsurf Communication has designed and developed the NRL/2019/5PNV protein supplement with micronutrient fortification for both male and female to help to manage health and quality of life.

It contains essential vitamin, minerals, herbal extracts together with a blend of whey, soy, pea, rice and milk solids. The current research depicts the efficacy and safety of the NRL/2019/5PNV with micronutrient fortification to promote health and wellbeing in healthy adults.

2. Material and Method

2.1 Investigational product details

Product Code: NRL/2019/5PNV. Key ingredients are Milk Solids, Maltodextrin, Protein blend (Whey Protein Concentrate, Soy protein isolate, Rice protein isolate, Pea protein isolate), DHA (omega 3-Algal source), *Aloe vera* extract, *Withania somnifera* extract, Minerals (Calcium phosphate tribasic, potassium citrate, sodium citrate, magnesium sulphate, ferric diphosphate, zinc sulphate, manganese sulphate, copper sulphate, sodium selenite), Vitamins (ascorbic acid, vitamin E, nicotinamide, calcium-D-pantothenate, pyridoxine hydrochloride, thiamine mononitrate, riboflavin, retinyl acetate, folic acid, d-biotin, phyloquinone, Vitamin D2 ergocalciferol, cyanocobalamin)

2.2 Study Design

A randomized, double Blind, controlled clinical study. The subjects were distributed randomly to test NRL/2019/5PNV treated and marketed product treated group. We had used

leading market brand as a protein supplement in comparator arm.

2.3 Study Objectives & Purpose

The primary objectives were assessment of daily activity questionnaire, endurance levels (steppers test), perceived stress levels, immunity via number of events of recurrent UTI/RTI etc., anthropometric analysis, HbA1c and glycemic profile ie blood sugar levels, regulation of lipid levels The secondary objectives were assessment of quality of life, changes in digestive behavior assessment, changes in mood behavior, safety profiling by LFT, RFT and thyroid profile etc., assessment of adverse events, changes in sleep quality questionnaire, palatability with dosage compliance of test product

3. Selection and Withdrawal of Subjects

3.1 Inclusion exclusion criteria

Inclusion Criteria for the study were: age group: 18 years - 65 years, BMI in the range of 20-26, subjects in good physical condition and sound mental status, in the judgment of the Principal Investigator, able to comply with protocol requirements, willing to sign written informed consent, subjects with willingness to abstain from use of vitamin or mineral supplements, nutritional supplements and or medical foods if applicable.

Exclusion Criteria for the study were: allergies to ingredients in product/ milk, Subjects with uncontrolled and uncomplicated diabetes (HbA1C NMT 7.0 % and blood pressure NMT 140/90 mm hg) may or may not be on prescription, subjects with past history of addiction abuse and rehabilitation, subjects with current medical history of any major illness such as cancer, heart disease, COPD, Asthma etc. in the past, subjects with history of any acute or chronic illness that may affect the patient's participation in the study, use of prescription medications and/or nonprescription medications for weight loss, subjects with acute illness or history of major or minor surgery in the past one year, female subjects who are currently pregnant and/or breast feeding, subjects not willing to participate in study

3.2 Recruitment Plan

We intended to complete 100 subjects (50 in each group) at the end of the study. Additional subjects were recruited to complete the required number (100) of completed subjects for analysis. Precautions have been taken not to recruit the subjects belonging to possible vulnerable groups.

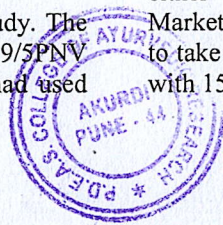
3.3 Withdrawal Criteria

Subjects withdrawn from the study for the following reasons: At their own request i.e. withdrawal of consent at any time for personal reasons. If, in the investigator's opinion, continuation in the study would be detrimental to the subject's well-being. Protocol deviations that could invalidate interpretation of the results (i.e. intake of not permitted concomitant treatments etc.)

4. Treatment of Subjects

4.1 Dosage and Treatment Duration

As per computer generated randomization list, subject was either be randomized to NRL/2019/5PNV (Test) or Marketed Product Group in 1:1 ratio. Subjects were advised to take given supplement in a dose of 10 gm in the morning with 150ml of milk for 90 days.



4.2 Visit Schedules

Subjects were asked to regularly visit at day 0, day 30, day 60 and day 90 of the treatment.

5. Measures taken to avoid bias

5.1 Randomization and study groups

All the subjects are randomly allocated (as per computer generated randomization list) to either one of the two treatment arms in 1:1 ratio. Subjects may be randomized to either NRL/2019/5PNV (Test) group or Marketed Product Group.

5.2 Blinding of the investigational products:

Identical comparator was provided as a marketed product. Primary packing of the test drug and standard was kept absolutely similar in order to keep both investigator as well as the subject blind.

6. Methodology

On screening visit, a written informed consent was obtained from the subjects for their participation in the study and their demographic details and vitals were recorded. The subject then proceeded to undergo clinical examination and their medical, surgical and treatment history was recorded. Current medication if any was noted in the case record from (CRF). The subject was considered for further evaluation as per the inclusion and exclusion criteria. Subject's blood sample were collected at the respective study centers for laboratory testing i.e. CBC, ESR, Hb%, Liver Function Tests, Lipid Profile, Renal Function test, HbA1c. During screening visit and the entire study duration subjects were advised to refrain from antioxidant agents, vitamins, anti-inflammatory drugs, hormones, Nutraceutical, Ayurvedic, Siddha, Unani, herbal /homeopathic medicines. On baseline visit, subject was recruited in the study if he or she met all the inclusion criteria. Subjects were then being to be randomized to one of the two study groups as per the computer generated randomization list. Subjects were asked for occurrence of any adverse event during screening period. Subject undergone clinical examination. Subject's Daily activity, Endurance levels (steppers test), Perceived stress levels and number of events of recurrent UTI/RTI etc. were recorded. Subject's Anthropometric analysis was performed. Following questionnaires were assessed like Quality of life (Physical, mental and social) General Health Questionnaire-28 (GHQ-28), digestive behavior assessment, mood behavior, sleep quality questionnaire. On every follow up visit the above said parameters were assessed. At baseline visit and at every follow up visit (except last follow up visit), as per computer generated randomization list, subjects were provided with investigational products. Subject were advised to consume given supplement in a dose of 10gms in the morning with 150 ml milk. Subject were advised to continue his/ her concomitant medication other than antioxidant agents, weight loss management, vitamins, anti-inflammatory drugs, hormones, Nutraceutical, Ayurvedic, Siddha, Unani, herbal /homeopathic medicines etc. The record of concomitant medication was kept in the CRF. Drug compliance was assessed by the investigator on every follow up visit. Subjects who continuously miss dosing for >3 consecutive days or total missed dose > 9 days during the study period were to be treated as drop outs.

There were no drop outs as of all were compliant. Subjects were advised to continue the diet and exercise regimen (which they are already following) during the entire study period.

On last follow up visit (i.e. Day 90) apart from all baseline assessments, subject's safety biochemical parameters along with the clinical examination were repeated. Adverse events were critically evaluated.

After completion of 3 months of study treatment, all the subjects were being asked to stop trial medications and take advice of investigator for further treatment.

All the subjects were closely monitored for any adverse event starting from baseline visit till the end of the study visit.

7. Ethical consideration and registration of study

7.1 Ethical Consideration

The study was initiated only after a written approval was from Independent/ Institutional Ethics Committee (IEC) and subsequent registration of study on CTRI website. The study was conducted as per approved protocol and as per Good Clinical Practices guidelines.

7.2 CTRI Registration

After getting approval from the ethics committee, the study was registered on CTRI website. Patients were enrolled in the study only after registration of study on CTRI website. The Registration details of study are- CTRI/2019/10/021716 [Registered on: 18/10/2019]-Trial Registered Prospectively.

8. Statistics

8.1 Sample size consideration

Sample size calculation is derived taking considerations of primary and secondary outcomes by a qualified statistician. The software used for calculation of sample size is SPSS version 10.0. There were 50 subjects recruited per group.

9. Results and observations

9.1 Demographic details

In the present study, 107 subjects were screened. Out of 107 subjects, 6 lost to follow up in the study. 101 subjects were considered evaluable cases at the end of the study 50 in test and 51 in marketed product treated group.

Out of 101 completed subjects, the mean age of Test group subjects in were 33.2 ± 6.83 years and the mean age of Marketed product group subjects was 33.38 ± 8.55 years. If compared between the groups, the difference was statistically insignificant.

The ratio of approximately 75:25 for male and female was decided and maintained during recruitment of the study.

9.2. Efficacy Assessments

9.2.1. Assessment of Maximum Aerobic Capacity (VO₂ Max)

There was non-significant difference between VO₂ Max calculated by 6MWT in Test product and Marketed product treated group at baseline. After day 60, there was significant increase in VO₂ Max calculated by 6MWT with test product treated group as compared to Marketed product. After day 90, there was significant increase in VO₂ Max calculated by 6MWT i.e. 24.64 ± 2.77 with test product treated group as compared to Marketed product.



Table 1: Assessment of Maximum Aerobic Capacity (VO₂ Max) between the groups

Duration (Days)	Mean VO ₂ Max (Mean± SD)	
	Test (N = 50)	Marketed Product (N = 51)
Baseline	20.80± 3.14	20.52± 3.23
30	20.95± 3.27	20.53± 3.23
60	22.59± 2.93*	19.80± 3.27
90	24.64± 2.77**	19.87± 2.71

ANOVA multiple comparison Test: P > 0.05 Not Significant; significant p< 0.01*, p<0.001**

9.2.2. Assessment of Mood Disorder Questionnaire (MDQ) Score

After day 90, there was significant (p<0.001) increase (2.56±0.62 and 1.80±0.66 respectively) between MDQ score in Test product and Marketed product treated group. In case of intergroup analysis, test product treated group demonstrated significant increase in MDQ score at day 60 and 90 when compared to baseline value of the same group. In case of intergroup analysis, marketed product treated group demonstrated non-significant increase in MDQ score at day 30, 60 and 90 when compared to baseline value of the same group.

9.2.3. Assessment of Pittsburgh Sleep Quality Index (PSQI)

There was non-significant difference between PSQI in Test product and Marketed product treated group at baseline. After day 60, and 90 there was significant decrease (p<0.01) in PSQI with Test product treated group.

Table 2: Assessment of Pittsburgh Sleep Quality Index (PSQI) between the groups

Duration (Days)	Mean Pittsburgh Sleep Quality Index (Mean± SD)	
	Test (N = 50)	Marketed Product (N = 51)
Baseline	10.87±5.55	10.09±3.12
30	9.76±3.17	9.82±3.04
60	6.13±1.96*	9.64±2.19
90	3.22±1.43**	10.18±1.27

ANOVA multiple comparison Test: P > 0.05 Not Significant; significant p< 0.01*, p<0.001**

9.2.4. Assessment of Perceived Stress Score (PSS):

There was non-significant difference between PSS in Test product and Marketed product treated group at baseline. After 30, 60 and 90 days there was significant decrease (p<0.001) in PSS evident with Test product compared to Marketed product treated group.

Table 3: Assessment of Perceived Stress Score (PSS) between the groups

Duration (Days)	Mean Perceived stress questionnaire (Mean± SD)	
	Test (N = 50)	Marketed Product (N = 51)
Baseline	24.73± 8.70	26.09± 3.67
30	19.91± 3.55**	25.18± 3.18
60	12.71± 2.94**	22.42± 3.58
90	5.29± 1.70**	24.71± 3.27

ANOVA multiple comparison Test: P > 0.05 Not Significant; significant p< 0.01*, p<0.001**

9.2.5. Assessment of General Health Questionnaire-28 (GHQ-28) Score

After day 60 and 90, there was significant increase

(p<0.001) in GHQ-28 score of Test product treated group compared to Marketed product treated group. During intragroup analysis both groups showed significant (p<0.05) increase in GHQ-28 score from their respective baseline values.

Table 4: Assessment of General Health Questionnaire-28 (GHQ-28) Score between the groups

Duration (Days)	Mean General Health Questionnaire-28 (Mean± SD)	
	Test (N = 50)	Marketed Product (N = 51)
Baseline	25.60±8.35	27.60±5.32
30	44.51±5.92	43.49±5.92
60	64.42±5.78**	58.02±9.17
90	80.04±2.26***	67.64±9.42

ANOVA multiple comparison Test: P > 0.05 Not Significant; significant p<0.001**, p<0.0001***

9.2.6. Assessment of Energy Audit Questionnaire

The frequency distribution of energy events depicted difference in "Very High" score is increased significantly in test treated group than marketed product treated group. The frequency distribution of energy events depicted difference in "High" score is increased significantly in test treated group than marketed product treated group. There was shift of events from low, neutral and moderate category of energy events to High and very high score.

The frequency distribution of energy events depicted that after treatment the number of subjects representing "High" and "Very High" energy level scores were increased and "Moderate" to "Very Low" energy levels were decreased. The similar results are evident from Mean Score of Energy Audit and frequency of energy events.

9.2.7. Assessment of Digestive Behavior Score

At day 30, 60 and 90 there was significant decrease in the mean score of bloating, constipation, loss of appetite and post prandial fullness in test treated group than marketed product treated group.

9.2.8. Assessment of Anthropometric parameters

According to the results obtained regarding anthropometric parameters of Test and Marketed product treated groups, it was observed that there is no significant difference in both the groups in parameters like body weight, circumferences, BMI and arm fat index etc. There was small increase in body weight (of average 1 to 1.5 kg in 3 months) in both the groups after treatment for 90 days but the difference was not significant.

There was significant reduction in fat % at day 90, in test group when compared to marketed product treated group. There was significant increase in the skeletal muscle % at day 90 in test group when compared to marketed product treated group.

9.2.9. Global assessment for overall improvement by investigator

In test group, 43 (86 %) subjects reported very much overall improvement and 07 (14 %) subjects reported much overall improvement at the end of the study.

In marketed product group, 04 (7.84%) subjects reported minimum overall improvement, 45 (88.23%) subjects reported no change and 01 (1.97 %) subject reported minimal worsening in the condition at the end of the study.

If compared between the groups, test treated group, performed significantly better than marketed product treated group.

9.2.10. Global assessment for overall improvement by subject

In test group, 45 (90 %) subjects reported very much overall improvement and 05 (10 %) subjects reported much overall improvement at the end of the study.

In marketed product group, 04 (7.84%) subjects reported minimum overall improvement, 45 (88.23%) subjects reported no change and 01 (1.97 %) subject reported minimal worsening in the condition at the end of the study. If compared between the groups, test treated group, performed significantly better than marketed product treated group.

9.2.11. Immunity events by recurrent RTI/ UTI

In test group, at baseline, 12 subjects of test group reported average of at least 12 events of RTI/ UTI in last month to commencement of project.

In test group, 10 subjects (20%) reported recurrent episodes of either RTI/UTI during three months' period. The number frequency of events were 13 events with two to three days' duration. Resolved completely before completion of the study duration.

In marketed product group at baseline, 10 subjects of test group reported average of at least 11 events of RTI/ UTI in last month to commencement of project. In marketed product group, 9 (17.64%) subjects reported 11 events of recurrent RTI/ UTI during three months' period and found to be completely resolved in two to three days. If compared between the groups, there was no significant change in both the groups.

9.3 Safety assessment

9.3.1. Changes in Mean parameters of Complete Hemogram, liver, renal, thyroid function test and random blood sugar levels

All the parameters in the complete Hemogram, liver, renal, thyroid function test and random blood sugar levels were within normal range and comparable between groups at baseline.

After treatment at day 90, mean value of parameters of said parameters did not show any significant change from baseline in test and marketed product treated groups. The difference was statistically insignificant.

9.3.2. Changes in Mean parameter of Lipid Profile

All the parameters of lipid profile were within normal limits at baseline visit in both the groups. After completion of the treatment, no significant change in all other parameters of lipid profile was observed in both the groups i.e. test and marketed product treated group apart from total cholesterol. There was significant $p < 0.05$ reduction in test product treated group at day 90.

9.3.3. Changes in Mean HbA1C

Change in Blood HbA1C levels were non-significant at baseline visit in both the groups. After completion of the treatment, there was significant decrease in HbA1C level in test treated group compared to marketed product treated groups.

Table 5: Changes in Mean HbA1C% between the groups

Duration (Days)	Mean HbA1c % (Mean $\pm$ SD)	
	Test (N = 50)	Marketed Product (N = 51)
Baseline	5.34 $\pm$ 0.97	5.30 $\pm$ 0.68
90	4.80 $\pm$ 0.46*	5.22 $\pm$ 0.08

Student's t test $P > 0.05$ Not Significant, $P < 0.05$ Significant

9.3.4. Changes in Vital parameters

Pulse, respiratory rate, blood pressure of subjects of both the groups was within normal limits at baseline visit. After completion of the treatment, no significant change in said parameters. If compared within the groups, the difference was statistically insignificant.

9.3.5. Tolerability of study drugs assessed by physician and subjects

As per physician and subjects, all the subjects (100%) from both the groups reported excellent tolerability to given intervention ie test product and marketed product.

9.3.6. Palatability and compliance

All the subjects ie 100% from both the groups reported excellent palatability and mix ability of the product. Both the groups also presented excellent compliance to both of the investigational products.

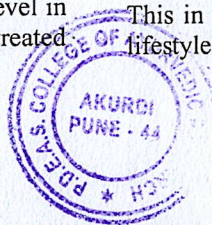
9.3.7. Profile of adverse events

In test group, 15 (30%) subjects reported a total of 17 adverse events during the study period. These adverse events included fever, menstrual pain, hyperacidity, injury, body ache, dry & irritable eyes, cold, heartburn and headache. All these adverse events were mild in severity except headache which was moderate in nature. These adverse events were resolved completely after rescue medication was given. Study treatment was not stopped during these adverse events. All these adverse events were not related to the study drug. In marketed product group, 11 (32%) subjects reported a total of 16 adverse events during the study period. These adverse events included fever, menstrual pain, headache, vomiting, lumbar pain, body ache, mouth ulcer and hyperacidity. All these adverse events were mild in severity and resolved completely after rescue medication was given. Study treatment was not stopped during these adverse events. All these adverse events were not related to the study drug. If compared between the groups, the difference was statistically insignificant.

10. Discussion

In the present study NRL/2019/5PNV was compared for its safety and clinical efficacy against Established Marketed Product. The interpretation of the study parameters obtained are expressed as follows.

VO₂ max, also known as maximal oxygen uptake which measures the maximum amount of oxygen a person can utilize during intense exercise. It is a common measurement used to establish the physical endurance of an individual before and after an oxygen requirement. Factors Affecting VO₂ max are genetics, age, lifestyle & fitness status and body composition. Shifting body composition to lean mass improvement can improve VO₂ max to considerable level. This in turn upgrades motivation to exercise/ activeness of lifestyle and thereby improving health status. VO₂ max



Directly measures body oxygen consumption, also get direct measurement of maximum heart rate by recording heart rate during the test. It is a measure of how well the heart and lungs work to deliver oxygen and energy to working muscles [40].

After day 60, there was significant increase in VO_2 Max calculated by 6MWT with test product treated group as compared to Marketed product. After day 90, there was significant increase in VO_2 Max calculated by 6MWT i.e. 24.64 ± 2.77 with test product treated group as compared to Marketed product.

Assessment of anthropometric parameters revealed following facts. There was slight increase (non-significant $p > 0.05$) in body weight in both NRL/2019/5PNV and marketed product treated groups. It was evident from results that there was significant decrease in body fat % i.e. 25.13 ± 6.84 in NRL/2019/5PNV vs. 27.95 ± 7.08 % at day 90 in Marketed product treated group. Though the body weight is slightly increasing in both groups, the fat content in NRL/2019/5PNV treated group decreases that contributes to its probable anabolic effect in improving skeletal muscle mass and %. It was clearly evident in comparison of skeletal muscle % at day 90 in both groups. Skeletal muscle % was 32.30 ± 8.97 in NRL/2019/5PNV and 29.02 ± 6.05 in marketed product treated group (Significant change $p < 0.05$), which indicates clinical superiority of NRL/2019/5PNV in positively modifying body composition by reducing body fat and improving skeletal muscle%. The same effect may be involved in improving VO_2 max by NRL/2019/5PNV.

The very practical and strong index of improving physical health and well-being is feeling of energy and stamina throughout the day. There was assessment of energy audit questionnaire to assess subjective changes of the energy levels of the subject divided in 4 parts of day i.e. early morning till breakfast, breakfast to lunch, lunch to evening snack time and late evening to bedtime. There was comparable baseline energy levels in both the treatment groups before starting of treatment. The energy levels were divided into Very high, High, Moderate, Neutral, Low and Very low depending on the expression of the energy at particular time [41]. The subject reported their reading in terms of score for the day. The results are expressed as mean score and frequency of events in each score title. There was significant increase in shift of individuals experiencing Very High and High energy evidences than Low, Moderate and Neutral energy level in NRL/2019/5PNV treated group than that of marketed product. Energy levels strongly depend on the digestion behavior and muscular strength and vitality together with mental state to perceive stress. The NRL/2019/5PNV contains plant based protein and herbal extracts of *Withania somnifera* and *Aloe vera*. The plant based proteins are easy to digest and could improve digestion cycle. *Withania somnifera* by virtue of its active constituents is known for its rejuvenating, anti-stress activity [42]. *Aloe vera* is known to potentially improve digestion by reducing gastric inflammation and mild laxative action [43]. The composition of NRL/2019/5PNV must have contributed to improve wellbeing of the subjects by improving their energy levels throughout the day.

After 30 and 60 days there was again non-significant difference between MDQ score in Test product and Marketed product treated group. After day 90, there was significant ($p < 0.001$) increase (ie 2.56 ± 0.62 and 1.80 ± 0.66

respectively) between MDQ score in NRL/2019/5PNV and Marketed product treated group. The NRL/2019/5PNV proved to be more efficacious in improving mood status in subjects than the marketed product. The effect could be attributed to the improved physical stamina, energy levels and rejuvenating effects of *Withania somnifera* as a combination [42, 44].

Quality of sleep determines physical, mental well-being and work productivity. It was demonstrable from the study that NRL/2019/5PNV is more efficacious in improving sleep quality in subjects. The assessment was performed by Pittsburgh Sleep Quality Index. The NRL/2019/5PNV showed significant $p < 0.001$ improvement in healthy uninterrupted sleep pattern in subjects. There is much stronger linkage in improvement of quality of sleep and energy levels. The relationship is witnessed in this research. The available scientific data support the conclusion that *Withania somnifera* is a real potent regenerative tonic (Rasayana of Ayurveda), due to its multiple pharmacological actions like anti-stress, neuroprotective, analgesic and anti-inflammatory etc. It is useful for prevention stress related sleep deprivation. The effect could be attributed to rejuvenating action of *Withania somnifera* [45].

Stress is psychological phenomenon and is greatly influenced by individual's ability to perceive the state of stress. The perception to the stress is largely dependent of lack of physical stamina, energy levels, digestion and healthy sleep pattern. NRL/2019/5PNV has demonstrated significant ($p < 0.05$) reduction in perceived stress score from 30 days of treatment up to 90 days when compared to marketed product. Protection to the human physiological system against diverse stressor, recent studies shows that the *Withania somnifera* having adaptogens which could induce a state of non-specific increase of resistance to affect internal homeostasis. The adaptogens improve the response to stress and help the body to adapt by normal physiological processes in times of increased stress. The anti-stress activity of *Withania somnifera* must have contributed through its adaptogenic action to combat stress situation. Antistress and adaptogenic properties of *Withania somnifera* have been investigated in all these studies using adult rats were carried out by swimming endurance stress test [42].

The right combination of essential vitamins and minerals are very important to keep the health and wellbeing to its maximum. NRL/2019/5PNV has blend of multivitamin and multiminerals to improve and restore the normal physiology of body and exert immunomodulatory and antioxidant potential. Omega 3 fatty acid present in NRL/2019/5PNV is known to restore cellular functioning, integrity and energy balance. Omega 3 fatty acids are cardio protective, neuroprotective nature.

It is well researched fact that protein's nutritional value also depends on its rate of digestion in the gastrointestinal tract. Whey proteins were digested more rapidly than casein. Whey proteins, which are highly soluble in acidic conditions, pass through the stomach and are rapidly hydrolyzed in the duodenum, causing rapid absorption. Soy proteins are digested faster than casein and are slower than whey proteins. Thus, the postprandial muscle protein synthesis rate is more in whey and soy proteins than milk proteins. Plant proteins like rice and pea proteins are not as good as improving anabolic effect but are easy to digest and

improve short term goals in body composition and help in skin, hair and nails health. It can adjust the overall digestibility of the protein blend [46].

After assessment of Digestive Behavior Score following were the observations. At day 30, 60 and 90 of treatment, there was significant decrease in the mean score of bloating, post prandial fullness and constipation ($p < 0.001$ respectively for 30, 60 and 90 days) in NRL/2019/5PNV treated group than marketed product treated group. At day 30, 60 and 90 there was significant decrease in the mean score of loss of appetite ($p < 0.001$ respectively for 30, 60 and 90 days) in test treated group than marketed product treated group. There is significant decrease in occasional abdominal pain and heartburn in NRL/2019/5PNV treated group as compared to marketed product, at day 90 ($p < 0.001$). The results suggest not only the ease in digestion of the NRL/2019/5PNV but also improvement in overall digestive behaviour. The attribution might go to the balanced blend of Whey, soya and plant based proteins like rice and peas together with goodness of *Aloe vera* as a digestive promoter.

Earlier epidemiological studies demonstrate that poor glycaemic control is an independent risk factor for CVD. Whey protein administration has been demonstrated to reduce postprandial glycaemia, mediated through various mechanisms including an enhancement of insulin secretion. Whey protein ingestion has also been shown to elicit an incretin effect, enhancing the secretion of glucose-dependent insulinotropic peptide and glucagon-like peptide-1, which may also influence appetite regulation and glycaemic control [47]. Soy protein is reported to possess low glycaemic index, suggesting that soy protein tend to improve control of blood glucose and insulin levels. Plant proteins like rice and pea proteins are reported to alter the glycaemic and appetitive responses as per a clinical trial conducted which help promoting glycaemic control [48]. The research evidence suggests a possible effect of *Aloe vera* on glycaemic control in prediabetes and type 2 diabetes.

In the present study, though random blood sugar is not significantly reduced, but the HbA1C levels are significantly reduced in NRL/2019/5PNV treated group than that of the marketed produce treated group. This can suggest possible potential of NRL/2019/5PNV in improving glycaemic control by virtue of the protein blend and herbal blend present in product.

Pre-diabetics are at risk of developing type-two diabetes. Many of the Indians are at risk of development of diabetes in near future as a result of borderline or higher levels of blood sugar and cholesterol levels. A randomized controlled trial with pre-diabetes reported reduction in the cholesterol levels after treatment of *Aloe vera* extracts [50].

The lipid-lowering effect of a soy-based protein supplement was evaluated by researchers in patients with hypercholesterolemia. It was evident that soy protein supplementation may effectively reduce serum cholesterol levels and therefore is likely to diminish the risk for cardiovascular disease. Previous studies have suggested that whey supplementation may have beneficial effects on lipid profile. Whey protein proved to be modest in lowering total cholesterol and triglycerides.

In the present study there was significant ($p < 0.05$) reduction in total cholesterol but no change in TG, HDL, LDL and VLDL in NRL/2019/5PNV treated group at day 90 of treatment.

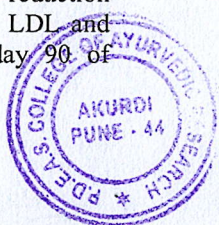
GHQ-9 is a standard questionnaire to assess Quality of Life. The assessment of the GHQ-9 score depicted that there was improved score at day 60 and 90 in NRL/2019/5PNV treated group than marketed product treated group.

11. Conclusion

NRL/2019/5PNV is safe and effective in promoting health and wellbeing in healthy adults. There was increased physical endurance by NRL/2019/5PNV treatment indicated as VO2 max compared to marketed product. This can be linked to exercise motivation, work efficiency and improved quality of life. The NRL/2019/5PNV was equally tolerated and compliant as that of marketed product. NRL/2019/5PNV was better in improving energy levels of the subjects throughout the day, elevating mood, improving quality of sleep. Together these parameters are true measures of wellbeing. NRL/2019/5PNV is promoting wellbeing and thus its consumption can elevate health status. NRL/2019/5PNV was found better in reducing the perception to the stress and thus improving quality of life. NRL/2019/5PNV improved digestive behavior of the subjects like reducing constipation, bloating, and loss of appetite and post prandial fullness. These are essentially complaints with sedentary lifestyle. NRL/2019/5PNV consumption is suitable for people with sedentary lifestyle experiencing digestive disturbances. There was improved glycaemic control indicated as significant reduction in HbA1C in NRL/2019/5PNV. A balanced blend of proteins like whey, soy, rice and peas along with proportionate vitamin and micro mineral fortification and addition of rejuvenating herbal extracts like *Withania somnifera* and *Aloe vera* is definitely providing better assimilation of the product and efficacy.

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विषय:- Clinical Trial for Protein supplements
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त्रिअल संपल्यानंतर त्यांचे sponsor कडून मिळालेले
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भा. मेलिया,

Mprex Healthcare आ CRO तर्फे आयुर्वेद कलाकर्म व र.न. हॉस्पिटल
द्वारे 2 Clinical Trials पुढे झाल्या.

① Randomised control trial to assess the efficacy & safety of
NPL/2019/SPNW with micronutrients fortification to promote
health & wellbeing in Women in fertile age
Protocol No - MHC/CT/19-20/007.

② Randomised control trial to assess the efficacy & safety of
NPL/2019/SPNV with micronutrients fortification to promote
health & wellbeing in healthy adults.
Protocol No - MHC/CT/19-20/006

आ दोन्ही त्रिअल मध्ये प्रत्येकी 10 subjects
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सह ① General Protein-Trial मध्ये

Dr. Ragini Patil - PI

Dr. Medha Joshi, Dr. Kurande - CO-I

② Woman Protein Trial मध्ये

Dr. Medha Joshi - PI

Dr. Ragini Patil, Dr. Kurande - CO-I

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Randomized Control Trial to Assess the Efficacy and Safety of NRL/2019/5PNW with Micronutrient Fortification to Promote Health and Well-being in Woman in Fertile Age

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ABSTRACT

Background: Women appear with gender specific nutritional requirements that may affect their well-being. The nutritional requirements are there for women in rural, suburban and urban regions altogether. **Objective:** Netsurf Communications Pvt. Ltd. has developed the NRL/2019/5PNW for the women to help manage their health and wellness. The current research is designed to assess safety and efficacy of the test product.

Methods and Materials: The trial is randomized, controlled prospective clinical trial. In the present study, 110 subjects were screened. Total 100 subjects were considered evaluable cases at the end of the study 1:1 in test and Marketed product treated group. **Results:** Test product was better in activity than marketed product in improving energy levels of the subjects throughout the day, elevating mood, improving quality of sleep and reducing stress. Improved glycemic control and reduction in total cholesterol levels

were significantly reduced in test group which has preventive potential of metabolic diseases. Less events of recurrent UTI/ RTI in test treated group suggestive of improvement in immune status of females.

Conclusion: NRL/2019/5PNW is safe and effective in promoting health and wellbeing in females in fertile age.

Key words: Curcumin, Energy level, Protein supplement, Soya, Whey.

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INTRODUCTION

A woman's nutritional and fitness requirements are different than men as there are indeed some special requirements of women to lose fat, gain muscle and look lean. Protein maintain cellular structures, hair, bones and connective tissue. Proteins account for digestive enzymes, immune system and muscle strength. Immune system functionality can be improvised by proper protein supplements. Bone health and density keeps bones strong and minimize the density loss that could be antickaging. Proteins help hair and nails looking healthy and strong thus improving wellness quotient.¹

Whey protein, soya protein together with vegetable proteins like rice, pea is a better blend in terms of presence of amino acids present and digestibility and thus assimilation. Plant-based proteins tend to be lower in calories and fat than animal proteins and higher in fiber and essential nutrients. Plant-based proteins made with peas can promote muscle thickness gains. In turn vegetable proteins help reducing hunger cravings, are easy at digestions and leads to less gastric distress than animal based source.²

Women have gender specific nutritional requirements that may affect wellbeing and there is great need to address the same. The requirements are there in rural, sub-urban and urban regions altogether. Anatomy and physiological stages of females and role of sex hormones throughout lifetime present nutritional challenges requiring special attention.³ Physical demands on females during fertile age affect nutrition, appetite and health status. Cultural and social factors resulting in stressing gender-specific roles, body shape and weight put woman on risk of

eating disorders and seeking unhealthy methods to lose weight. Neural and hormonal factors associate to mood swings and perception to stress in woman life.⁴ Women present many nutrition-related concerns from weight maintenance to bone health. By taking in to consideration the special need of good protein for women, the Netsurf Communications Pvt. Ltd. has designed and developed the NRL/2019/5PNW for the women to help to manage health and wellness. The present study aims and clinical validation of safety and efficacy of woman protein supplement in their fertile age.⁵

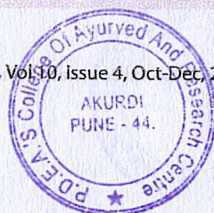
MATERIALS AND METHODS

The study was initiated after Ethics Committee approval and subsequent registration of study on CTRI website (CTRI/2019/10/021717 [Registered on: 18/10/2019]). The study was conducted as per Good Clinical Practices guidelines. Patients were enrolled in the study only after registration of study on CTRI website.

The primary objectives of the study were to evaluate efficacy of NRL/2019/5PNW and marketed product in fertile women by assessing-daily energy levels, menstrual regulation, changes in biochemical parameters, immunity via number of events of recurrent UTI/RTI etc., changes in hormonal profile.

The secondary objectives of the study were to assess- quality of life (Physical, mental and social) General Health Questionnaire-28 (GHQ-28), changes in mood behavior, sleep quality questionnaire, perceived stress questionnaire, safety assessment.

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Inclusion Criteria

Fertile Women Aged 18 – 50 years with BMI in the range of 20–26 Kg/m² were incorporated. Subjects having good physical condition and sound mental status and in the judgment of the principal investigator, able to comply with protocol requirements were included. Subjects willing to sign written informed consent and willing to abstain from use of additional vitamin or mineral supplements, nutritional supplements and or medical foods if applicable were recruited in the trial.

Exclusion Criteria

Subjects with medical history of any major illness such as cancer, heart disease, COPD, Asthma etc. in the past were excluded. Subjects with history of any acute or chronic illness that may affect the patient's participation in the study were excluded. Subjects on prescription medications and/or nonprescription medications for weight loss were not considered in the study. Pregnant and/or breast feeding subjects, not willing to participate in study, subjects with history of hysterectomy, IUI and IVF Subjects with PCOS and or on any hormone replacement therapy were excluded. NRL/2019/5PNW powder is approved by FSSAI. It contains protein blend (whey protein concentrate, soy protein isolate, pea protein isolate, rice protein isolate), milk solids DHA (omega 3-Algal source), curcumin, shatavari extract, multivitamins and multiminerals.

As per computer generated randomization list, subject were either be randomized to test or marketed product group in 1:1 ratio. Dose of 10 gm. in the morning with 150ml of milk for 90 days were administered. Visit schedule were on baseline visit, day 30, 60 and 90.

Study procedure

Fertile female subjects of age between 18 to 50 years of age (both inclusive) attending outpatient department of study site(s) were screened for eligibility criteria. On screening visit, a written informed consent was obtained from subjects for their participation in the study. Subject's demographic details and clinical examination was recorded. Subject's medical, surgical and treatment history was taken. Subject's current medication if any was noted in the case record from (CRF). The subject was considered for further evaluation as per the inclusion and exclusion criteria. All biochemical parameters were recorded at screening visit. During screening visit and the entire study duration subjects were advised to refrain from antioxidant agents, vitamins, anti-inflammatory drugs, hormones, Nutraceutical, Ayurvedic, Siddha, Unani, herbal / homeopathic medicines. Subjects were checked for occurrence of any adverse event during screening period. Subject's daily energy levels, changes in menstrual regulation, anthropometric analysis and immunity events were assessed. Subjects were assessed for follow up visits after every month up to 3 months. On last visit the biochemical tests were repeated. All clinical and questionnaires were assessed for all visits. All the subjects were closely monitored for any adverse event.

Table 1: Assessment of Mood Disorder Questionnaire (MDQ) Score between the groups.

Duration (Days)	Mean Mood Disorder Questionnaire (Mean ± SD)	
	Test (N = 50)	Marketed Product (N = 50)
Baseline	2.04±0.51	1.98±0.63
30	2.04±0.47	2.00±0.48
60	2.41±0.54**	2.02±0.40
90	2.47±0.50**	2.08±0.46

By ANOVA Test: $P > 0.05$ Not Significant; significant $p < 0.01^*$, $p < 0.001^{**}$

Sample size consideration

Sample size calculation is derived taking considerations of primary and secondary outcomes by a qualified statistician. The software used for calculation of sample size is SPSS version 10.0

RESULTS

Demographic details

In the present study, 110 subjects were screened. Out of 110 subjects, 3 subjects were screen failure and 7 lost to follow up in the study. 100 subjects were considered evaluable cases at the end of the study 50 in test and 50 in Marketed product treated group.

Out of 100 completed subjects, the mean age of Test group subjects in were 35.67 ± 8.01 years and the mean age of Marketed product group subjects was 34.38 ± 7.36 years. If compared between the groups, the difference was statistically insignificant.

Assessment of mood disorder questionnaire (MDQ) score

There was significant ($p < 0.001$) increase in MDQ score in Test product compared to Marketed product treated group after day 60 and 90. The results are given in Table 1.

Assessment of Pittsburgh sleep quality index (PSQI):

There was significant decrease ($p < 0.001$) between PSQI in Test product and Marketed product treated group after day 60 and 90. The results are given in Table 2.

Assessment of perceived stress score (PSS)

There was significant decrease ($p < 0.001$) between PSS in Test product and Marketed product treated group after day 60 and 90. The results are given in Table 3.

Assessment of general health questionnaire-28 (GHQ-28) score

At 30, 60 and 90 days there was significant ($p < 0.001$) increase in GHQ-28 score of Test product compared to Marketed product treated group. The results are given in Table 4.

Assessment of energy audit questionnaire

The frequency distribution of energy events depicted difference in "Very High" and "High" score is increased significantly in test treated group than marketed product treated group. The results are given in Table 5.

Assessment of anthropometric parameters

There were significant ($p < 0.05$) reduction in fat % at day 60 and 90, in test group when compared to marketed product treated group. There

Table 2: Assessment of Pittsburgh Sleep Quality Index (PSQI) between the groups.

Duration (Days)	Mean Pittsburgh Sleep Quality Index (Mean ± SD)	
	Test (N = 50)	Marketed Product (N = 50)
Baseline	5.52±2.57	5.48±2.43
30	4.28±2.40	5.43±2.37
60	2.48±1.47**	4.85±2.44
90	2.04±0.84**	4.95±3.47

By ANOVA multiple comparison Test: $P > 0.05$ Not Significant; significant $p < 0.01^*$, $p < 0.001^{**}$

were significant ($p < 0.05$) reduction in visceral fat % at day 60 and 90, in test group when compared to marketed product treated group. There was small increase in body weight in both groups after treatment but the comparison was not significant.

Assessment of iron profile

There was significant ($p < 0.05$) increase in serum iron in test group when day 90 results (73.45 ± 22.51) were compared to baseline results (69.14 ± 27.02) of same group. There was significant ($p < 0.05$) increase in ferritin levels at day 90 between test and marketed product treated group. The mean values of ferritin were 51.34 ± 5.98 and 45.27 in test and marketed product treated group respectively.

Assessment of hormonal profile

The hormonal ranges were normal in all subjects and there was no significant changes in serum levels of FSH, LH, PRL and testosterone after treatment with test and marketed product treated group.

Assessment of immunity events by recurrent RTI/ UTI

Total of 15 subjects of test group reported average of 15 events of RTI/ UTI prior to last month of trial commencement. Total 10 subjects (20%) reported recurrent episodes of either RTI/UTI during three months period. Total 12 subjects of marketed product treated group reported average of at least 13 events of RTI/ UTI prior to last month of trial commencement. In marketed product group, 15 (30) subjects reported 18 events of recurrent RTI/ UTI during three months period and found to be completely resolved in two to three days.

Assessment of menstrual profile

Total 5 subjects out of 50 ie 10% of test group subjects' experiences profuse blood flow at baseline of which only 2 subjects were reporting profuse blood flow after 3 months of treatment with test product. In case of marketed product, 4 out of 50 of marketed product group subject's

experienced profuse blood flow at baseline and 5 subjects were reporting profuse blood flow after 3 months of treatment with test product.

Changes in Mean parameters of complete hemogram, liver, renal, thyroid function test, serum insulin and random blood sugar levels

All the parameters in the complete hemogram, liver, renal, thyroid function test, serum insulin and random blood sugar levels were within normal range and comparable between groups at baseline. After treatment at day 90, mean value of parameters of said parameters did not show any significant change from baseline in test and marketed product treated groups. The difference was statistically insignificant.

Changes in mean parameter of lipid profile

There was significant $p < 0.05$ reduction in total cholesterol of test product treated group at day 90. The results are given in Table 6.

Changes in mean HbA1C

After completion of the treatment, there was significant decrease in HbA_{1c} level in test treated group compared to marketed product treated groups. The results are given in Table 7.

Changes in vital parameters

Pulse, respiratory rate, blood pressure of subjects of both the groups was within normal limits at baseline visit. After completion of the treatment, no significant change in said parameters.

Tolerability of study drugs assessed by physician and subjects

As per physician and subjects, all the subjects (100%) from both the groups reported excellent tolerability to given intervention i.e test product and marketed product.

Profile of adverse events

There were 20 (40%) and 18 (36%) subjects reported a total of 24 and 26 adverse events during the study period respectively in test and marketed product treated group. These adverse events included fever, menstrual pain, hyperacidity, injury, body ache, urinary irritation, cold, heartburn and headache. These adverse events were resolved completely after rescue medication was given. Study treatment was not stopped during these adverse events. All these adverse events were not related to the study drug.

DISCUSSION

Women of reproductive age experience many emotional disturbances, of which 20-50% percent have a broad symptomatology. These emotional distress could be a sign of premenstrual syndrome that could be not distinguished presentation so far. Mood fluctuations are very common and profound symptom in many woman which affects her quality of life. The irritable and depressed moods alters the perception to the stress triggers and develop perceived stress.⁶ In the present study NRL/2019/5PNW found to be significant in improving mood status in females than in marketed product treated group from day 60. The activity of the NRL/2019/5PNW would be due to improved energy levels due to protein intake and micronutrients supplementation like vitamins and minerals.

Women show up with poorer sleep quality than men and possess risk for insomnia. Disturbed sleep could be attributed to reproductive hormones, stress, depression, aging, societal and family liabilities.⁷ Reduced Pittsburgh Sleep Quality Index indicated that the NRL/2019/5PNW

Table 3: Assessment of Perceived Stress Score (PSS) between the groups.

Duration (Days)	Mean Perceived stress questionnaire (Mean $\pm$ SD)	
	Test (N = 50)	Marketed Product (N = 51)
Baseline	17.50 $\pm$ 3.34	18.18 $\pm$ 3.18
30	17.17 $\pm$ 2.51	17.52 $\pm$ 3.05
60	11.93 $\pm$ 3.43**	17.52 $\pm$ 3.14
90	11.63 $\pm$ 4.53**	18.36 $\pm$ 4.96

By ANOVA multiple comparison Test: $P > 0.05$ Not Significant; significant $p < 0.01^*$, $p < 0.001^{**}$

Table 4: Assessment of General Health Questionnaire-28 (GHQ-28) Score between the groups.

Duration (Days)	Mean General Health Questionnaire-28 (Mean $\pm$ SD)	
	Test (N = 50)	Marketed Product (N = 50)
Baseline	42.70 $\pm$ 9.62	47.61 $\pm$ 5.38
30	57.41 $\pm$ 8.34**	43.43 $\pm$ 5.98
60	71.39 $\pm$ 6.04***	58.82 $\pm$ 9.18
90	78.98 $\pm$ 5.55***	61.84 $\pm$ 9.44

By ANOVA multiple comparison Test: $P > 0.05$ Not Significant; significant $p < 0.001^{**}$, $p < 0.0001^{***}$

Table 5: Assessment of Energy Audit Questionnaire Mean Score between the groups.

Energy Level	Mean Energy Audit(Mean $\pm$ SD)					
	Test (N=50)			Marketed Product (N=50)		
	Day 30	Day 60	Day 90	Day 30	Day 60	Day 90
Very High	4.00 $\pm$ 3.93	23.35 $\pm$ 11.13	24.46 $\pm$ 7.61	3.91 $\pm$ 4.00	10.73 $\pm$ 8.69	14.02 $\pm$ 5.34
High	5.96 $\pm$ 4.85	31.52 $\pm$ 10.15	27.96 $\pm$ 7.26	6.05 $\pm$ 4.45	19.43 $\pm$ 14.81	23.41 $\pm$ 7.73
Moderate	35.35 $\pm$ 13.70	27.11 $\pm$ 9.62	23.61 $\pm$ 7.77	34.09 $\pm$ 14.57	37.66 $\pm$ 10.93	32.84 $\pm$ 9.00
Neutral	38.39 $\pm$ 15.09	24.61 $\pm$ 9.86	20.78 $\pm$ 6.14	39.11 $\pm$ 15.76	37.82 $\pm$ 14.44	25.70 $\pm$ 9.05
Low	15.22 $\pm$ 10.37	7.78 $\pm$ 4.80	2.57 $\pm$ 2.40	15.23 $\pm$ 10.93	8.77 $\pm$ 5.24	2.59 $\pm$ 2.35
Very low	19.93 $\pm$ 21.28	4.67 $\pm$ 3.91	0.91 $\pm$ 1.98	20.36 $\pm$ 21.25	5.18 $\pm$ 4.73	0.86 $\pm$ 1.64

By ANOVA multiple comparison Test: $P > 0.05$ Not Significant; significant $p < 0.001^{**}$, $p < 0.0001^{***}$

Table 6: Changes in Mean parameters of lipid profile between the groups.

Lipid Profile	Mean(Mean $\pm$ SD)			
	Test (N = 50)		Marketed Product (N = 50)	
	Baseline	Day 90	Baseline	Day 90
Total Cholesterol (mg/dl)	164.22 $\pm$ 28.42	155.26 $\pm$ 32.62*	166.91 $\pm$ 30.20	169.70 $\pm$ 25.40
Cholesterol HDL Direct (mg/dl)	54.57 $\pm$ 11.69	52.96 $\pm$ 13.54	56.17 $\pm$ 11.92	55.35 $\pm$ 12.52
Triglycerides (mg/dl)	126.84 $\pm$ 59.50	129.53 $\pm$ 58.75	129.70 $\pm$ 38.94	128.80 $\pm$ 45.05
LDL Cholesterol (mg/dl)	103.65 $\pm$ 20.61	101.76 $\pm$ 25.69	108.12 $\pm$ 18.11	106.93 $\pm$ 16.65
VLDL Cholesterol (mg/dl)	25.98 $\pm$ 10.09	27.38 $\pm$ 10.42	26.56 $\pm$ 9.43	28.26 $\pm$ 10.44

By Student's t Test: $P > 0.05$ Not Significant, $P < 0.05$ Significant*

treated group experiences less disturbed sleep with less mid night awakenings and sleep latency however improved onset of sleep and duration of uninterrupted sleep etc.

One of the most widely used tool for measuring the perception of stress is the Perceived Stress Scale (PSS). This scale evaluates the degree to which situations in one's life are judged as stressful.⁸ At day 60 and 90, NRL/2019/5PNW demonstrated significant reduction in PSS suggestive of lesser appraisal of stress in situations of life by subjects treated with NRL/2019/5PNW. The reduced perception to stress could be due to reduced mood fluctuations, improved sleep and energy levels.

The assessment of the GHQ-9 score depicted that there was improved score at day 30, 60 and 90 in NRL/2019/5PNW treated group than marketed product treated group.

Physical health and well-being is feeling of energy and stamina. There was assessment of energy audit questionnaire to assess subjective changes of the energy levels of the subject divided in 4 parts of day i.e. early morning till breakfast, Breakfast to lunch, Lunch to evening snack time and late evening to bedtime. The energy levels were divided into Very high, High, Moderate, Neutral, Low and Very low depending on the expression of the energy at particular time.⁹ The subject reported their reading in terms of score for the day. The results are expressed as mean score and frequency of events in each score title. There was significant increase in shift of individuals experiencing Very High and High energy evidences than Low, Moderate and Neutral energy level in NRL/2019/5PNW treated group than that of marketed product. Energy levels are strongly depend on the muscular strength and vitality together with improved mood status and reduced perceived stress.

Excessive visceral fat is associated with decreased insulin sensitivity which in turn increases risk to cardiovascular disease. In case of woman the visceral fat can induce deposition of reproductive hormone and thus potentiates risk of PCOD etc.¹⁰ The reduction in visceral fat in

Table 7: Changes in Mean HbA1C% between the groups.

Duration (Days)	Mean HbA1c %(Mean $\pm$ SD)	
	Test (N = 50)	Marketed Product (N = 50)
Baseline	5.17 $\pm$ 0.49	5.15 $\pm$ 0.52
90	4.68 $\pm$ 0.51*	5.18 $\pm$ 0.54

Student's t test : $P > 0.05$ Not Significant, $P < 0.05$ Significant*

NRL/2019/5PNW treated group can prove beneficial in preventing these complications.

Ferritin is a protein that stores iron. Ferritin are present in hepatocytes and reticuloendothelial cells. The ferritin binds to another substance called transferrin. It combines with ferritin to transport it to where new red blood cells are made. It's not only important to have normal iron levels, but should have enough stored iron. From the data of present study it is demonstrated that NRL/2019/5PNW improved ferritin levels significantly at day 90 than marketed product. In the data obtained in study, serum iron, total iron binding capacity and transferrin % are increased in both groups magnitude wise but non-significant in comparison. Iron helps to preserve many vital functions in the body, including general energy and focus, gastrointestinal processes, the immune system and the regulation of body temperature. It indicated the ability of NRL/2019/5PNW to improve iron profile in fertile females. This could lead in improved energy, stamina and health status.

As there are positive changes in the energy, stamina, mental state and quality, there are positive changes in immunity status as indicated by events of URI/ RTI in treatment months.

Recent research evidence that curcumin has strong anti-inflammatory and antioxidant activities and modulates inflammatory responses

which are underlying cause to many diseases. Curcumin possess immunomodulatory effects with multilayer response such as effect on lymphoid cell populations, antigen presentation, humoral and cell-mediated immunity and cytokine production. Curcumin present in NRL/2019/5PNW can play good role in modifying immunity of subjects.¹¹ NRL/2019/5PNW possess extract of *Asparagus racemosus* ieshatavari. The roots of shatavari are tonic and diuretic and galactagogue and possess ulcer healing effect probably via strengthening the mucosal resistance or gastro-cytoprotection. *A. racemosus* is widely used from ancient times in keeping woman health by virtue of antihepatotoxic, immunomodulatory effects, immune adjuvant effect, uterine tonic and general tonic and rejuvenator properties.¹² Glycemic regulation is thought to be a key in maintaining healthy metabolism and preventing many metabolic diseases like diabetes, cardiovascular diseases. Protein supplements changes all paradigm of metabolism and manages to get good glycemic conditions when person is not on high fat diet.¹³ Soy protein is reported to possess low glycemic index. Plant proteins like rice and pea proteins are reported to alter the glycemic and appetitive responses.¹⁴ In the present study, though random blood sugar is not significantly reduced, but the HbA_{1c} levels are significantly reduced in NRL/2019/5PNW treated group.

It was evident that soy protein supplementation may effectively reduce serum cholesterol levels and therefore is likely to diminish the risk for cardiovascular disease.¹⁵ In the present study there was significant ($p < 0.05$) reduction in total cholesterol in NRL/2019/5PNW treated group at day 90 of treatment.

CONCLUSION

In comparison to marketed product with a protein blend with multivitamin, NRL/2019/5PNW showed marked improvement in stress score, sleep pattern, glycemic control than marketed product. NRL/2019/5PNW produced reduction in cholesterol levels and visceral fat than marketed product. There was no significant post treatment change in biochemical tests in both the groups, suggesting both the drugs were safe in human subjects. Thus NRL/2019/5PNW is safe and effective in promoting health and wellbeing in fertile females.

ACKNOWLEDGEMENT

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CONFLICT OF INTEREST

There are no conflicts of interest.

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Tentative Budget for Clinical Trial.

Protein Supplement for Healthy children
(Age group 6 to 12 yrs.)

Department I. Kaumashalya. (Balrog)

Principle investigators - $35 \text{ pts} \times 1,000 = \text{Rs. } 35,000/-$

Co-investigators - $35 \times 500 = \text{Rs. } 17,500/-$

JRF - Total - $\text{Rs. } 10,000/-$

IEC Fee - $\text{Rs. } 20,000/-$

Miscellaneous charges $\text{Rs. } 05,000/-$

Institutional charges $\text{Rs. } 10,000/-$

$\text{Rs. } 97,500/-$

Deodas
(Dr Deodas M.S.)



दि. १४/१०/१९.

प्रति,
भा. रुग्णालय अधीक्षक
ARSMH, निगडी, पुणे ज. ४४.

आयुर्वेद शास्त्र	स्वीकृतशाली
आवक क्र. 1635/19-20	44.
दिनांक - 16/10/19	
लेखनिक	✓

विषय :- Clinical trial घेण्याची परवानगी मिळवितात.
विभाग :- कौमारभृत्य (बालरोग विभाग)
संदर्भ :- Maprex Healthcare या Sponsor २०२ कर्तर्फे
Protein Supplement to Healthy children
age group 6 to 12 yrs. या Clinical trial
बाबत.

आ. महोदया,
उपरोक्त संदर्भित पत्र व विषयास अनुसरून
MAPREX Healthcare च्या मंड. गायत्री गानु यांनी
उपरोक्त trial आपल्या रुग्णालयात घेण्याविषयीचे पत्र
पाठविले आहे. व या Clinical trial घेण्यासाठीची
परवानगी व Budget देण्याची विनंती त्यांनी केली आहे
सदर trial ची माहिती खालील प्रमाणे -

Sponsor - MAPREX Healthcare.

Subject for Trial - 30 + 5

Duration of Trial - 3 months + 1 month for inclusion

Budget for trial - Total Rs. 1,00,000/-

(Details attached)

सरी सदर Clinical trial घेण्याची परवानगी मिळवी,
सर्वेच Ethical Committee द्वारा मंजुरी मिळवी, ही नम्र
विनंती.

आपल्या मार्गदर्शनाचे व पुढील कार्यवाहित्व सादर.

Forwarded ✓



आ वि.
Dr. Deodas
(Dr. Deodas M.S.)
Prof & Head
Balrोग Dept.

1st Phase trial consent.



MPREX HEALTHCARE PVT. LTD.

Office Number 501, Crossroads, Bhumkar Square, Wakad, Pune – 411057
E: clinical@mprex.in, research@mprex.in, www.mprex.in

Date: 26/12/2020

To:

Dr. Madhavi Deodas

P.D.E.A.s Ayurved Rugnalay and Sterling hospital, Nigdi, Pune

Ref: Protocol no. NRL/2019/5PNK

Subject: Study Close-out Visit for Randomized control trial to assess the efficacy and safety of NRL/2019/5PNK with micronutrient fortification to promote growth, health and wellbeing in children.

Dear Dr. Madhavi Deodas

This letter is to confirm Study Close-out Visit for the above listed protocol conducted at your site. Following data is verified over accuracy of information and compliance related to the protocol:

- CRFs, medical charts, and consent documents for all enrolled subjects
- Investigator's Site File
- Investigational Product Supply/Dispensing Records

This letter is issued by undersigned as the gesture of the conclusion of the close out visit, any outstanding issues, and to review your continuing investigator obligations.

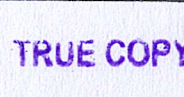
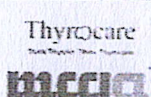
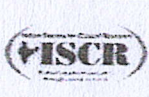
The Clinical Study Report is submitted along with the letter.

Please do not hesitate to contact for any concerns or questions.

Sincerely,

P. Bhalerao

Dr. Puja Bhalerao
Dept. Medical Affairs
Mprex Healthcare Pvt. Ltd.



Principal
College of Ayurved And Research Centre
Akurdi, Pune - 411 044

A randomized controlled trial to assess the efficacy and safety of children's health supplement with micronutrient fortification to promote growth, health, and wellbeing in children

Priya Khare¹, Omkar Kulkarni¹, Anuj Agrawal¹, Gayatri Ganu², Madhavi Deodas³

¹Netsurf Research Labs Pvt. Ltd, Pune, Maharashtra, India, ²Clinical Research Unit, Mprex Healthcare, Pune, Maharashtra, India, ³Pune District Education Association, Pune College of Ayurveda and Sterling Hospital Research Center, Pune, Maharashtra, India

Abstract

Background: Proteins are one of the strong pillars of sound physical health and cognitive abilities. Protein and micronutrient deficiency can hamper the health and growth of many children globally, delaying their physical and mental improvement and increase proneness to infections. The current research depicts the efficacy and safety of the children's health supplement with micronutrient fortification to promote growth, health, and wellbeing in children. A multicenter randomized controlled trial. **Material and Methods:** Two centers one being a teaching institute with a hospital and the second one private hospital. Total 105 subjects visiting the out patient department (OPD) section participated of which 100 completed the trial with five being dropped out as lost to follow-up. Children's health supplement (NRL/2019/5PNK) contains essential vitamins, minerals, herbal extracts together with a blend of whey, soy, pea, rice proteins, and milk solids. It was consumed as 90 days' treatment in a dose of 10 g daily with 150 mL milk. Children's health supplements improved anthropometric parameters and growth of children indicated by height-to-age and weight-to-age z-scores defined by world health organization (WHO). **Results:** There was a 45.70% increased physical endurance by children's health supplement. Enhanced immunity status indicated by reduced illness episodes and missed school days. Children's health supplements improved child's eating behavior and cognitive performance better than the marketed product. It was found better in improving digestive behavior in children. **Conclusion:** Children's health supplement found safe and effective in promoting growth, health, and wellbeing in healthy children.

Keywords: Nutrition, physical endurance, wellbeing, z-score

CTRI/2019/11/021993-Registered Prospectively.

INTRODUCTION

Scientific background and rationale

Protein and micronutrient deficiency can impede the health and growth of many children globally. It can delay their physical and mental improvement and increase proneness to infections. Protein deficiency could result in a negative nitrogen balance. Essential amino acids contribute the most to the mental and physical health of the child. There are several symptoms of protein deficiency that often are overlooked such as fatigue, lack of concentration, slowed growth, and lowered immunity. As per a study conducted by

Abbott Laboratories, one in seven school-aged children in the US is not consuming enough protein; the numbers are almost double in developing countries like India.^[1] Protein nutrition is one of the strong pillars of sound physical health and

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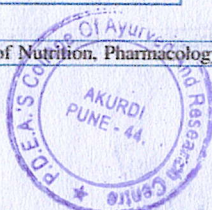
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cognitive abilities.^[2] Undernutrition with proteins and infection is a vicious cycle, along with deteriorating illness and declining nutritional status. Protein undernutrition could be the main cause of the immunocompromised state, such children are more prone to gastrointestinal (GI) and respiratory infections, and it is important to consider opportunistic infections such as viruses, gram-negative bacteria, fungal, and parasitic infestations. Undernutrition, low growth rate, overweight, micronutrient deficiencies, and osteopenia are nutritional confounders that affect the impairment neurologically.^[3]

The stage of growth in children is defined by the attributes of height and weight. For attaining the same, all nutrients must be ingested, absorbed, metabolized, and excreted properly since better assimilation translates to nutritional sufficiency. In the case of children, their metabolism is a constantly evolving mechanism and not a fixed combination that could work, but easy digestibility will make difference in better assimilation.^[4] Families with a low socioeconomic status often have little access to micronutrient-rich foods like fruits, vegetables, meat, fish, and dairy. In affluent profile families, protein malnourishment can result from excessive ingestion of fatty, carbohydrate, and sugar-rich food.^[5] A wide range of traditional as well as contemporary health products is available for children and the pressure is on the homemaker to keep the health of the children up to the mark. There is a great need for a researched product with proven safety and effectiveness to completely rely on the product for child consumption.

Netsurf Communications Pvt. Ltd. has developed children's nutraceutical supplement (NRL/2019/5PNK, henceforth will be termed as test product) containing protein with micronutrients fortification, with a natural product designed to promote general health and wellbeing of children, to support the optimum natural growth and development of children, enhanced immunity, and to the maintenance of adequate natural cognitive function. It contains essential vitamins, minerals, herbal extracts together with a blend of whey, soy, pea, rice, and milk solids. It is in powder form, 10 g of it is mixed in water or milk for consumption. The current research depicts the efficacy and safety of the test product with micronutrient fortification to promote growth, health, and wellbeing in children.

Study hypotheses

The hypothesis of the research was "Was test product as effective as the marketed comparator in safety and efficacy and were there any additional benefits of test product against the marketed product to promote growth, health, and wellbeing in children?"

MATERIAL AND METHODS

Trial design

The study was a randomized, double-blind, parallel-arm, controlled clinical trial. The subjects were randomized to test the product or marketed product (market comparator)

group (comparator is the leading brand of protein supplement for children) in a 1:1 ratio.

Ethical consideration

The study was initiated only after written approval is obtained from the Independent Ethics Committee (IEC) and subsequent registration of the study on the clinical trial registry of India (CTRI) website. The study was conducted as per approved protocol and as per Good Clinical Practices guidelines.

Data availability and CTRI registration

After getting approval from the ethics committee, the study was registered on the CTRI website. Patients were enrolled in the study only after registration of study on the CTRI website. The Registration details of the study are: CTRI/2019/11/021993 [registered on November 13, 2019] – Trial Registered Prospectively.

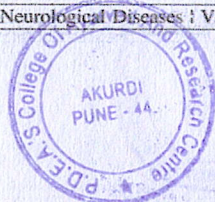
Selection criteria of subjects

The subjects along with their guardians/parents visiting out patient department (OPD) of the two trial sites were screened for the inclusion and exclusion criteria for the said trial. The subjects who fulfilled inclusion criteria and did not meet any exclusion criteria had been selected to participate in the trial.

Inclusion criteria for the study were: children aged 6 to 11 years inclusive (both gender), providing consent by an understanding of the study and willingness to participate as evidenced by subject's parents and/or legal guardian's voluntary written informed consent; ready for compliance; and is willing, able, and likely to comply with all study procedures and restrictions.

Exclusion criteria for the study

Following were the exclusion criteria: the subject with a known allergy or intolerance to the study product or ingredients, on a special diet and cannot consume the study product, subject with a current illness requiring hospitalization, subject with a GI infection and/or acute diarrhea at the time of inclusion in the study, and the subject on medication that could affect absorption/metabolism of study product. The subject is diagnosed with recurrent respiratory infections due to cystic fibrosis, active tuberculosis, acute hepatitis B or C or HIV, malignancy (as per history in the medical records) were excluded, as per discretion of investigation; subject with a history of diabetes (as per history and documentation in the medical records), subject been on antibiotic therapy within the last 1 month before the start of the study (before study day 1), subject with dysphasia, aspiration risk, and difficulty in swallowing due to acquired/congenital abnormalities that would hamper oral intake of the study product were excluded (as per history and documentation in the medical records); subject with a clinically significant nutritional deficiency requiring specific treatment with any other nutritional supplement (not study product) as diagnosed by the investigator were excluded for the safety concern.



responsiveness, eating speed (reduced sluggishness after treatment), emotional undereating (got reduced after treatment) in test product treated group than marketed product treated group as shown in Table 3.

Table 1: Assessment of maximum aerobic capacity (VO₂ max) between the groups

Duration	Mean VO ₂ max	
	Test	Marketed product
Baseline	40.18 ± 3.96	41.20 ± 4.96
Day 30	42.59 ± 3.60	42.90 ± 4.62
Day 60	48.87 ± 3.96	47.32 ± 4.70
Day 90	58.50 ± 4.69*	52.32 ± 2.33

By one-way ANOVA followed by Bonferroni selective multiple comparison test: $P > 0.05$, not significant. ANOVA, analysis of variance.

Assessment of Emotional Intelligence Questionnaire

The Emotional Intelligence Questionnaire was assessed based on the response from the subject's parent/guardian. After day 90, there was significant ($P < 0.0001$) improvement in scores of the following domain of the questionnaire, such as social skills, motivation, self-regulation, self-awareness, and empathy in test product treated group than marketed product treated group as shown in Table 4.

Assessment of Evaluation of Development and Behavior Questionnaire

The Development and Behavior Questionnaire was assessed based on the response from the subject's parent/guardian. After day 90, there was a significant improvement

Table 2: Assessment of WHO z-score

WHO z-score	Mean WHO z-score (Mean ± SD)							
	Test				Marketed product			
	Baseline	Day 30	Day 60	Day 90	Baseline	Day 30	Day 60	Day 90
Height-to-age (z-score)	-0.89 ± 1.40	-0.66 ± 1.34	-0.60 ± 1.29	-0.51 ± 1.29	-1.10 ± 1.37	-0.79 ± 1.41	-1.68 ± 1.51	-1.58 ± 1.29
Weight-to-age (z-score)	-1.33 ± 1.48	-1.29 ± 1.45	-1.06 ± 1.47	-0.89 ± 1.10	-1.46 ± 1.58	-1.35 ± 1.58	-1.28 ± 1.92	-0.95 ± 1.41

By one-way ANOVA followed by Bonferroni selective multiple comparison test: $P > 0.05$, not significant. *Symbol represents that results are significant i.e. P value < 0.05 . ANOVA, analysis of variance; WHO, world health organization; SD, standard deviation.

Table 3: Assessment of Child Eating Behavior Questionnaire between the groups

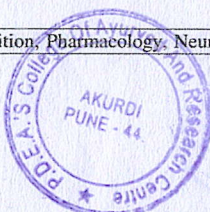
Questionnaire	Mean Child Eating Behavior Questionnaire score (Mean ± SD)			
	Test		Marketed product	
	Baseline	Day 90	Baseline	Day 90
Food responsiveness	11.16 ± 2.41	6.27 ± 1.05 [†]	10.53 ± 2.83	11.59 ± 3.76
Emotional overeating	10.55 ± 2.11	6.38 ± 1.68 [†]	10.32 ± 1.88	10.29 ± 1.82
Enjoyment of food	7.27 ± 1.63	16.47 ± 1.10 [†]	7.19 ± 1.52	9.53 ± 3.34
Desire to drink	8.30 ± 1.32	11.07 ± 0.75 [†]	8.48 ± 1.34	9.39 ± 1.40
Satiety responsiveness	19.55 ± 1.45	12.56 ± 1.78 [†]	19.59 ± 1.81	19.45 ± 14.68
Slowness in eating	15.60 ± 1.34	10.77 ± 1.24 [†]	15.36 ± 2.24	14.29 ± 2.39
Emotional undereating	15.26 ± 2.47	7.67 ± 1.93 [†]	14.86 ± 2.82	13.52 ± 3.17
Food fussiness	16.55 ± 2.23	18.33 ± 1.22	15.48 ± 3.86	18.42 ± 2.79

By one-way ANOVA followed by Bonferroni selective multiple comparison test: $P > 0.05$, not significant. [†] $P < 0.001$. *Symbol represents that results are significant i.e. P value < 0.05 . ANOVA, analysis of variance; SD, standard deviation.

Table 4: Assessment of Emotional Intelligence Questionnaire (EIQ) between the groups

Questionnaire	Mean Emotional Intelligence Questionnaire score (Mean ± SD)			
	Test		Marketed product	
	Baseline	Day 90	Baseline	Day 90
Social Skills	6.02 ± 1.04	8.07 ± 0.75 [†]	5.91 ± 0.95	6.00 ± 0.99
Motivation	5.17 ± 1.81	8.27 ± 0.84 [†]	5.44 ± 1.18	5.74 ± 1.16
Self-regulation	4.67 ± 1.51	7.93 ± 0.94 [†]	4.81 ± 1.38	5.26 ± 1.26
Self-awareness	4.39 ± 0.86	7.89 ± 0.91 [†]	4.18 ± 1.24	6.31 ± 1.04
Empathy	3.98 ± 1.44	8.07 ± 0.72 [†]	4.07 ± 1.35	7.60 ± 11.18

By one-way ANOVA followed by Bonferroni selective multiple comparison test: $P > 0.05$, not significant. [†] $P < 0.001$. *Symbol represents that results are significant i.e. P value < 0.05 . ANOVA, analysis of variance; SD, standard deviation.



($P < 0.0001$) in all domains of Development and Behavior score in test product than marketed product treated group as shown in Table 5.

Assessment of anthropometric parameters

According to the results obtained regarding anthropometric parameters of test and marketed product treated groups, it was observed that there is no significant difference in both the groups in parameters like body weight, circumferences, body mass index (BMI), arm fat index, etc. In the within-group analysis, test product and marketed product treated group showed significant improvement ($P < 0.05$) in

anthropometric parameters at day 90 compared to baseline reading with height, weight, and BMI as shown in Table 6.

Changes in mean serum BDNF level

Mean serum BDNF levels were within normal limits at baseline visit in both the groups. After completion of the treatment, no significant change in serum BDNF level was observed in both the groups, that is, test and marketed product treated groups. If compared within the groups, there was a nonsignificant improvement in serum BDNF when 90 days readings were compared to baseline values of the respective groups as shown in Table 7.

Table 5: Assessment of Evaluation of Development and Behavior score between the groups

Development and behavior	Mean Emotional Intelligence Questionnaire score (Mean $\pm$ SD)			
	Test		Marketed product	
	Baseline	Day 90	Baseline	Day 90
Motor skills – gross motor skills	8.91 $\pm$ 1.77	18.20 $\pm$ 1.42 [†]	9.05 $\pm$ 1.33	14.31 $\pm$ 1.87
Attention and concentration	11.79 $\pm$ 1.32	20.67 $\pm$ 2.01 [†]	11.62 $\pm$ 1.45	13.62 $\pm$ 2.21
Overactivity and impulsivity	14.05 $\pm$ 2.06	22.31 $\pm$ 2.07 [†]	13.70 $\pm$ 2.45	14.78 $\pm$ 1.82
Passivity/inactivity	6.48 $\pm$ 0.92	12.20 $\pm$ 1.36 [†]	6.64 $\pm$ 1.06	8.44 $\pm$ 1.20
Planning/organizing	5.49 $\pm$ 0.86	10.73 $\pm$ 1.03 [†]	5.58 $\pm$ 0.85	7.73 $\pm$ 1.30
Perception of space and directions	6.52 $\pm$ 0.99	12.58 $\pm$ 1.14 [†]	6.66 $\pm$ 0.86	7.91 $\pm$ 1.28
Perception of visual forms and figures	5.66 $\pm$ 1.08	11.00 $\pm$ 0.88 [†]	5.62 $\pm$ 0.94	7.82 $\pm$ 1.25
Memory	13.45 $\pm$ 4.41	24.04 $\pm$ 2.74 [†]	13.23 $\pm$ 1.75	15.98 $\pm$ 1.84
Comprehension of spoken language	6.79 $\pm$ 0.86	12.16 $\pm$ 1.04 [†]	7.16 $\pm$ 2.06	9.07 $\pm$ 2.02
Verbal communication	4.64 $\pm$ 1.83	8.24 $\pm$ 0.86 [†]	4.77 $\pm$ 2.92	6.00 $\pm$ 1.24
Acquisition of academic skills	12.66 $\pm$ 1.38	25.53 $\pm$ 1.83 [†]	12.20 $\pm$ 1.93	15.30 $\pm$ 2.70
Social skills	13.93 $\pm$ 1.53	27.53 $\pm$ 2.30 [†]	14.02 $\pm$ 1.47	15.82 $\pm$ 2.04
Emotional issues handling	17.79 $\pm$ 1.73	36.98 $\pm$ 2.71 [†]	17.80 $\pm$ 2.51	19.20 $\pm$ 2.47
Obsessive actions or thoughts	8.57 $\pm$ 2.47	5.27 $\pm$ 1.81 [†]	8.70 $\pm$ 2.50	9.62 $\pm$ 1.81

By one-way ANOVA followed by Bonferroni selective multiple comparison test: $P > 0.05$, not significant. [†] $P < 0.001$. *Symbol represents that results are significant i.e. P value < 0.05 . ANOVA, analysis of variance; SD, standard deviation.

Table 6: Assessment of anthropometric parameters between the groups

Parameters	Mean (Mean $\pm$ SD)			
	Test		Marketed product	
	Baseline	Day 90	Baseline	Day 90
Height (cm)	126.19 $\pm$ 10.65	131.76 $\pm$ 10.77	124.34 $\pm$ 10.22	128.29 $\pm$ 11.10
Weight (kg)	24.13 $\pm$ 6.14	26.75 $\pm$ 4.59	23.87 $\pm$ 6.71	26.82 $\pm$ 12.22
Waist circumference (cm)	22.94 $\pm$ 2.45	23.48 $\pm$ 2.11	22.86 $\pm$ 2.42	23.45 $\pm$ 1.09
Hip circumference (cm)	26.17 $\pm$ 2.18	26.42 $\pm$ 2.30	26.01 $\pm$ 3.05	26.40 $\pm$ 1.88
Upper arm circumference (cm)	7.34 $\pm$ 0.96	7.82 $\pm$ 1.34	7.56 $\pm$ 8.68	7.98 $\pm$ 3.77
Triceps skinfold thickness (cm)	14.57 $\pm$ 5.77	17.71 $\pm$ 18.10	14.53 $\pm$ 5.58	16.39 $\pm$ 4.66
Head circumference (cm)	19.93 $\pm$ 1.12	20.80 $\pm$ 1.08	20.01 $\pm$ 1.45	20.44 $\pm$ 1.19
Chest circumference (cm)	23.48 $\pm$ 2.32	23.76 $\pm$ 2.26	23.32 $\pm$ 2.27	23.97 $\pm$ 2.32
Foot length (cm)	26.82 $\pm$ 3.41	27.20 $\pm$ 3.10	26.04 $\pm$ 3.60	26.88 $\pm$ 3.20
Arm length (cm)	15.78 $\pm$ 1.98	16.23 $\pm$ 2.88	15.58 $\pm$ 2.71	15.90 $\pm$ 1.50
Body mass index	14.65 $\pm$ 2.07	15.22 $\pm$ 2.93	15.26 $\pm$ 2.79	15.91 $\pm$ 2.10
Body fat %	7.52 $\pm$ 6.05	8.06 $\pm$ 4.09	8.69 $\pm$ 6.51	9.08 $\pm$ 7.10

By one-way ANOVA followed by Bonferroni selective multiple comparison test: $P > 0.05$, not significant. ANOVA, analysis of variance; SD, standard deviation.

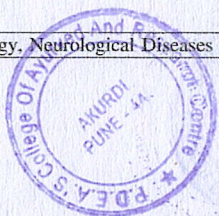


Table 7: Changes in mean serum iron level between the groups

Duration(days)	Mean serum BDNF (pg/mL)(Mean $\pm$ SD)	
	Test	Marketed product
Baseline	583.92 $\pm$ 96.93	594.82 $\pm$ 89.92
90	597.63 $\pm$ 92.38	608.39 $\pm$ 98.38

Student *t* test; *P* > 0.05, not significant. BDNF, brain-derived neurotrophic factor. SD, standard deviation.

DISCUSSION

Physical fitness is an indicative sign of health in children and adolescents. For instance, low fitness levels are associated with a higher risk of developing obesity, cognitive disorders, and musculoskeletal weakness later in life. In this study, to assess the physical endurance, a modified 20 m PREFIT project framework was utilized. There were correlations and equations based on heart rate, distance covered, and velocity of running in the stipulated distance. It will give us a fair idea about the cardiovascular fitness of children.^[6] In the present study, after day 90, there was a significant increase (*P* < 0.05) in VO₂ max calculated by PREFIT test with test product treated group as compared to marketed product. There was 45.70% VO₂ max improvement in the test product treated group compared to 21.25% improvement in the marketed product treated group. The results are indicative of muscle strength improvement and thus physical stamina.

WHO recognizes a system by which a child or a group of children can be compared for the rate of growth, to the reference population: *z*-scores (standard deviation scores), percentiles, and percent of median.^[7,8] For population-based assessment including surveys and nutritional surveillance, the *z*-score is widely recognized as the best system for analysis and presentation of anthropometric data because of its advantages compared to the other.^[9] Mainly height-to-age and weight-to-age are interpreted by using the *z*-score classification system as a great indicator of growth rate and its adequacy. The *z*-score system expresses the anthropometric value as several standard deviations or *z*-scores below or above the reference mean or median value.

The current WHO recommendation is to use the *z*-score for grading undernutrition. Children who are with 1 standard deviation (SD) below the reference median, that is, around -1 are borderline undernourished, more than 2 SD below the reference median (i.e., a *z*-score of less than -2) are considered to be undernourished, that is, to be stunted, wasted, or to be underweight. Children with measurements below 3 SD (a *z*-score of less than -3) are considered to be severely undernourished.^[10]

In the present study, children who represented marginal undernourishment though were not having severe symptoms and were randomly sampled. There was a nonsignificant difference in height-to-age and weight-to-age *z*-score in the test product and marketed product treated group at baseline.

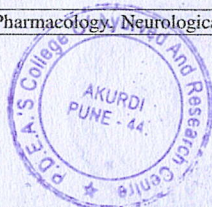
After 30, 60, and 90 days there was a nonsignificant difference in height-to-age and weight-to-age *z*-score between the test product and marketed product treated group. The *z*-score as height and weight indicator with age were improving in magnitude but the comparison was nonsignificant. In the case of intragroup analysis, the test product treated group and marketed product treated group demonstrated significant improvement in height-to-age and weight-to-age *z*-score at day 30, 60, and 90 when compared to a baseline value of the respective group. It indicated that the test product was equally good in promoting the growth rate of the child.

Dietary habits are shaped at a young age and maintained during later life with tracking over time. Eating behaviors established in childhood persist, with implications such as fussiness, undernourishment, or obesity. It is very important thus to check if the dietary supplement in terms of the blend of macro- and micronutrients are offering some sort of positive impact in child's eating behavior.^[8] In the present study, the behavior is assessed through a well-researched and validated Child Eating Questionnaire. There are a set of questions to be assessed from the parent/guardian of the child in the following domain: food responsiveness, emotional overeating, enjoyment of food, desire to drink, satiety responsiveness, sluggish eating, emotional under-eating, etc. The response can measure the eating habit and role of nutritional supplement in improving this domain to get positive and nourishment contained eating habits.

In the present study, after day 90, there was a significant (*P* < 0.001) improvement in scores of all domains in the test product treated group compared to the marketed product treated group. There is an important consideration of better absorption and assimilation of nutrients from nutritional supplements to bring about changes in the eating habits in the child as a result of nutritional sufficiency. It can be concluded that the test product proved better to alter the eating habits and behavior in children than the marketed product.

The appetite score was assessed and found to be improved in both test and marketed product treated groups. Almost 70% of parents of subjects from both the groups complained of less appetite on the baseline for their children. But there was a significant difference in appetite score after day 60 and day 90 in the test and marketed product treated group. It shows test product better performing to improve appetite which will inculcate good eating habits thus optimal food response to avoid under- and overeating in children.

It is a well-researched fact that there is a correlation between emotional intelligence and eating misbehavior in school-going children. The emotional quotient and intelligence is the major key component in the development of child to grow as a socially responsible person. Emotional intelligence is related to the following domains: social skills, motivation, self-regulation, self-awareness, and empathy.^[11] The questionnaire assessing the emotional intelligence domain was implemented in the present study to be answered by



the parent or guardian of the subject to come to the score representing the emotional intelligence orchestra of the child. It was found that after day 90, there was significant ($P < 0.0001$) improvement in scores of the following domain of the questionnaire: such as social skills, motivation, self-regulation, self-awareness, and empathy in the test product treated group than marketed product treated group. This is indicative of the potential of the test product to find a link between physical nutrition and psychological soundness. The result could be due to the improved eating pattern, appetite, nutritional sufficiency by the supplement, and joint effort of *Brahmi* (*Bacopa* extract) from the test product as it is reported to possess effectiveness in improving the psychosomatic functionalities at an early age.^[12]

The overall development of the child is quite incomplete without cognitive and behavioral development in the right way. These aspects are studied in this research through a standard questionnaire involving a set of questions to be answered by the parent or guardian of the child. There are strong links between macro- and micronutritional sufficiency and behavior and cognitive development. In turn, better cognition and behavior uplift a child's self-image and thus train the self-esteem to take newer challenges and develop.

Gross motor skills are helping the child to be active, competitive, and alert in group or isolation and require physical and mental stamina which can be built by a correct nutritional supplement. Attention and concentration not only help the child to improve in academics but also can cultivate nature to work in a team. Children with attention deficit could face a lot many psychosocial challenges in the later stages of their lives. On the contrary to this overactivity through less attention, the extreme polar condition is passivity and child's tendency of being passive and not taking interest in the academics as well as interactive opportunities. It could be reversed by counseling and therapies but the nutritional balance and omega supplements can play a key role in improving this condition. Planning, perception to space, and visual forms and figures are the part of the neurological development of a child to perform more complex processes in the later stage of life along with verbal and spoken language communications. Cognitive development performs a pivotal role in child development and always is a major concern from the parent's perspective.

With the current results of scores of the questionnaire in the present study, it could be concluded that all the set of developmental parameters are better improved (significance: $P < 0.001$) at day 90 by test product when compared to the marketed product. Academic and social skill scores were also improved in the test-treated product than the marketed product.

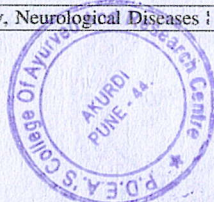
Bacopa monnieri, popularly known as *Brahmi*, has been traditionally used in Ayurveda for ages for its memory-enhancing properties. The reported study which planned to evaluate the effect of *B. monnieri* on the memory of students for 6 weeks revealed improved memory, both visual as well

as verbal.^[13] *B. monnieri* is reported to improve working memory and short-term verbal memory in children.^[14]

According to the results obtained regarding anthropometric parameters of test and marketed product treated groups, it was observed that there is an increase in height, weight, BMI, circumferences of chest, waist, and head, etc., as the children are under growing phase but no significant difference in both the groups in parameters like body weight, circumferences, BMI, and arm fat index, etc.

As a clinical measure of the immune status of the children, we had considered episodes of recurrent respiratory tract infection (RTI) and illness episodes as a scale. Following are the results of the current study: in the test group, at baseline, 20 subjects of the test group reported an average of at least 20 events of RTI in the previous month. On the contrary, 10 subjects (20%) reported recurrent episodes of RTI during 3 months period. The number frequency of events was 10 events with 2 to 3 days duration and was resolved completely before completion of the study duration. In the test group, the total missed days of the subjects were 13 days.

In the marketed product group, at baseline, 15 subjects of the test group reported an average of at least 18 events of RTI in the previous month whereas nine (17.64%) subjects reported 12 events of recurrent RTI during the 3 month test period and was found to be completely resolved in 2 to 3 days and total missed days of the subjects were 15 days. If compared between the groups, there was no significant change in both the groups. Test product improved immune status of the child by reducing illness episodes and thus the missed school days as a result of protein sufficiency and development of strength to combat the infections. *Ashwagandha* extract used in the test product is thought to be an excellent immunomodulator in action. It is reported to possess anti-inflammatory, antioxidant values. Many clinical trials have witnessed the usefulness of *Ashwagandha* to promote both innate and acquired immunity.^[15] The micronutrient supplementation like vitamin C and D in the test product has immunity-building potential. Colostrum used as an ingredient in test products possesses immunity modifying properties that could contribute to the ability to cope up with.^[16,17] BDNF is a protein of the neurotrophin family. It is expressed in human brains. It is associated with synaptic plasticity, connectivity, and neuroprotection. It also serves an important role during neurological development through the regulation of neural circuit development. BDNF plays an important role in learning and memory at an early age. It is found in most concentrations in the hippocampus region of the brain. BDNF is an important factor in neurodevelopment. It is reported in a research that serum BDNF may present an inverse correlation with the intelligence, attention, and cognition of preschool children with neurodevelopmental disorders such as intellectual disability, and attention-deficit/hyperactivity disorder (ADHD) can very well be correlated to abnormal free peripheral BDNF.^[18] In the present study, the serum BDNF levels in both the group



were within the normal range at baseline and did not produce any significant change after treatment with test and marketed product treatment for 90 days.

As an assessment of adverse event profile, there was no significant difference in both groups. Both groups represented mild adverse event episodes like fever, injury, dry and irritable eyes, cold, muscle pain, etc. All these adverse events were mild in severity. These adverse events were resolved completely after 1 to 3 days with rescue medication. Study treatment was not stopped during these adverse events. All these adverse events were not related to the study drug. Global assessment for overall improvement by subject parent/guardian and investigator revealed that children's health supplement demonstrated much-very much overall improvement in both treatment groups. Excellent tolerability of both the drugs was reported by subjects and physicians at the end of the study. No significant post-treatment change in any of the laboratory investigations was observed in both the groups like complete hemogram, liver, kidney, lipid, and thyroid profile tests. In the present study, there were nonsignificant changes in random blood sugar and hemoglobin A1c (HbA1c) in children's health supplement treated and marketed product treated group. There is no significant change in serum calcium levels in both groups. In the present study, there was a significant ($P < 0.05$) reduction in total cholesterol but no change in triglycerides (TG), high density lipoprotein (HDL), low density lipoprotein (LDL), and very low density lipoprotein (VLDL) in the children's health supplement treated group at day 90 of treatment. There was no significant posttreatment change in vitals such as pulse rate, blood pressure, body temperature, and respiratory rate was observed in both the groups, suggesting both the drugs were safe in human subjects. Thus children's health supplement with micronutrient fortification is safe and effective in children. Children's health supplements and marketed products both presented excellent palatability and mixability with milk. There was 100% compliance for both children's health supplements and marketed products by subjects during the study. The trial complies external validity, also called generalizability as these results can be generalized in population as the broader inclusive criteria yet potentially excluding the subjects may prove inappropriate for the study had made the generalization feasible.

CONCLUSION

The children's health supplement is safe and effective in promoting growth, health, and wellbeing in healthy children. It improved the growth of children indicated by height-to-age and weight-to-age z-scores defined by WHO was comparable with the marketed product. Height, weight, BMI, and circumferences of chest, waist, and head were increased as an indicator of child's physical growth in children's health supplement as well as marketed product treated groups. There

was 45.70% increased physical endurance by children's health supplement treatment indicated as VO_2 max compared to baseline. This can be linked to physical stamina. Enhanced immunity status was indicated by reduced illness episodes and missed school days in children's health supplement and marketed product treated groups. Children's health supplement improved child's eating behavior better than the marketed product. It reduced fussy eating; also food responsiveness and satiety of food score as per the questionnaire was improved after children's health supplement treatment as compared to marketed product. Emotional intelligence score was better in children's health supplement treatment than the marketed product. Improved cognitive performance was seen in children's health supplement treatment than the marketed product. The children's health supplement was found better in activity than the marketed product counterpart in improving digestive behavior in children.

Financial support and sponsorship

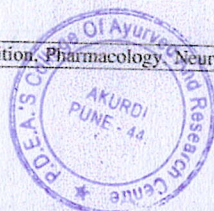
This study was funded by Netsurf Communications Pvt. Ltd.

Conflicts of interest

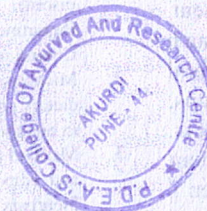
There are no conflicts of interest.

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CONCLUSION

The children's health supplement is safe and effective in promoting growth, health and well-being in healthy children. It improved the growth of children and helped in the management of various health issues. The study also showed that the supplement helped in the management of various health issues. The study also showed that the supplement helped in the management of various health issues. The study also showed that the supplement helped in the management of various health issues.

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Plate-A, 2nd Floor,
Office Block-III, NBCC Complex,
East Kidwai Nagar, ND-23

Dated: 17th July, 2020

To

The Pay & Accounts Officer (Sectt.),
Ministry of Health & Family Welfare,
Nirman Bhawan, New Delhi.

Sub: - Release of Grants-in-aid of Rs.8,12,070/- as 1st installment for SARS CoV-2 infection and COVID 19 disease under Modified Extra Mural Research (EMR) Scheme during 2020-21-reg.

Sir,

In exercise to powers delegated under DFPR-1978, I am directed to convey the sanction of the President of India for release of an amount of Rs.8,12,070/- (Rupees Eight Lakhs Twelve Thousand & Seventy Only) to "P.D.E.A's Ayurveda Rugnalaya and Sterling Multispecialty Hospital, Pune" as 1st installment of recurring grants for the Research Project titled "Clinical trial to evaluate prophylactic action of Twakadi Herbal Tea in Police professionals working in Covid-19 pandemic" under EMR Scheme during the year 2020-21.

2. The Sanction has been issued as per Rules 228 to 245 of General Financial Rules – 2017. The grant-in-aid will be subject to the conditions and provisions of the modified EMR Scheme for SARS CoV-2 infection and COVID 19 disease and no amount or part thereof shall be delivered/utilized to any other purpose than the one for which it has been sanctioned.
3. The accounts of the grantee institution/organization shall be open to inspection by the sanctioning authority and audit both by the CAG of India under the provisions of CAG (DPC) Act, 1971 and internal audit wing of the O/o CCA of the Ministry, whenever the institution or organization is called upon to do so.
4. The Grants-in-aid of Rs.8,12,070/- (Rupees Eight Lakhs Twelve Thousand & Seventy Only) is a recurring grants.
5. This sanction is subject to condition that the grantee institute will disburse this grant-in-aid through EAT (Expenditure, Advance and Transfer) Module of PFMS as per the guidelines under Ministry of Finance
6. The sanction is issued subject to conditions that information/details in respect of Direct Benefit Transfer (DBT) under the budget heads Salary/Manpower and TA/DA as per notification of the Scheme under Section 7/57 of Aadhaar Act 2016 will be provided/uploaded to this Ministry on monthly basis as per DBT App/Format by the Principal Investigator/Organization.
7. The expenditure is debitable to the Demand No. 4- Ministry of AYUSH, 2210-Medical and Public Health (Major Head), 2200-Other System (Minor Head), 07-Grants for Extra Mural Research Projects through Research Institute (Pvt./Semi-Govt./University/NGO's etc.), 070031-Grants-in-aid (General) during 2020-21. Scheme Code (3121-EMR).
8. No Utilization Certificate is pending against this institute during previous years under this scheme.



(Signature)

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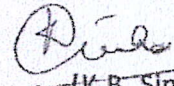
(Signature)
Principal

College of Ayurved And Research Center,
Akurdi, Pune - 411 044

Contd.....2/-

9. This issues with the approval of the IFD concurrence Dy. No. C- 151 dated 09.07.2020.

Yours faithfully,

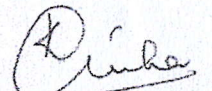

(K.B. Sinha)

Under Secretary to the Govt. of India

Copy forwarded for information and necessary action to:

1. The Director General of Audit, Central Revenues, I.P. Estate, New Delhi-110002.
2. Niti Aayog, (Health Division), Sansad Marg, New Delhi.
3. SO (IFD-AYUSH), M/o H&FW, Nirman Bhavan New Delhi.
4. Cash (AYUSH) Section for preparing bill.
5. DDG (P&E), Ministry of AYUSH, New Delhi.
6. Sanction Register.
7. The P.D.E.A's Ayurveda Rugnalaya and Sterling Multispecialty Hospital, Pune - with the request that the above released grants should mandatorily be disbursed only through EAT (Expenditure, Advance and Transfer) Module of PFMS as per the guidelines under Ministry of Finance.
8. Prof. Dr. Yogini Ramachandra Kulkarni, Ayurveda Consultant, PG Director & HOD Research, P.D.E.A's Ayurveda Rugnalaya and Sterling Multispecialty Hospital, Pune

आयुष मंत्रालय
Ministry of AYUSH
आयुष भवन, बी-ब्लॉक, अपराध संशोधन भवन
AYUSH Bhawan B-Block GPO Complex INA New Delhi


(K.B. Sinha)

Under Secretary to the Govt. of India

N.B.

The Institute will submit/maintain the following documents in connection with the above grants: -

1. Utilization Certificate as per the provision of Scheme Guidelines & as per prescribed format of GFR-2017 (i.e. GFR-12A).
2. Audited Statement of Expenditure indicating accrued interest, if any, on the released grants.
3. Detailed Research Project Report against the released grants.
4. The Head of the Institute shall be personally accountable for proper utilization of the grants.
5. The grant is being released as 1st installment for the Research Project titled "Clinical trial to evaluate prophylactic action of Twakadi Herbal Tea in Police professionals working in Covid-19 pandemic.
6. The details of approved budget for the above project are as under: -

Heads	Total	1st installment	10 % withheld amount
Manpower SRF-01 @ Rs.35,000/- per month + HRA @ 16 % Rs.5600/- = Rs.40,600/-	Rs.1,21,800/-	Rs.1,21,800/-	-
Medicines (including standardization)	Rs.31,000/-	Rs.31,000	-
Laboratory investigations	Rs.6,69,500/-	Rs.5,94,270	Rs.75,230
PPE Kits	Rs.60,000/-	Rs.60,000/-	-
Data Analysis	Rs.10,000/-	-	Rs.10,000/-
Stationary and Misc. cost	Rs.10,000/-	Rs.5,000/-	Rs.5,000/-
Total	Rs.9,02,300/-	Rs.8,12,070/-	Rs.90,230/-



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Principal

College of Ayurved And Research Centre,
Akurdi, Pune - 411 044

No. S.14011/6/2020-Scheme (EMR)
Government of India
Ministry of Ayurveda, Yoga & Naturopathy, Unani, Siddha & Homoeopathy

Plate -A, 2nd Floor,
Tower-III, NBCC Office,
East Kidwai Nagar-110023
Dated: 7th Dec., 2021

To,

The Pay & Accounts Officer (Secretariat),
Ministry of Health and Family Welfare,
Nirman Bhawan, New Delhi-110011.

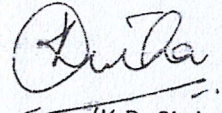
Sub: - Utilization Certificate of Rs.8,12,070/- against grants released to **P.D.E.A's Ayurved Rugnalaya and Sterling Multispeciality Hospital, Pune** as 1st installment under the Central Sector Scheme for SARS CoV-2 infection and COVID-19 disease under Modified Extra Mural Research (EMR) Scheme during 2020-21.

Sir/Madam,

I am directed to certify that out of total released grants of Rs.8,12,070/- (Rupees Eight Lakhs Twelve Thousand & Seventy Only) sanctioned/released to **P.D.E.A's Ayurved Rugnalaya and Sterling Multispeciality Hospital, Pune** as 1st installment, vide this Ministry's Sanction Order No. **S.14011/6/2020-Scheme (EMR) dated 17.07.2020**, an amount of **Rs.8,07,066/-** (Rupees Eight Lakhs Seven Thousand & Sixty-Six Only) has been utilized for the purpose for which it was sanctioned. The remaining **unutilized amount** of **Rs.5,004/-** (Rupees Five Thousand & Four only) refunded by the organization has been deposited in Govt. Account vide Challan No. 72 dated 22.06.2021. The Competent Authority is satisfied that the condition on which the grant was sanctioned have been duly fulfilled on the basis of the Utilization Certificate & supporting documents furnished by the Institute.

2. The expenditure was debited under Demand No. 4- Ministry of AYUSH, 2210-Medical and Public Health (Major Head), 2200-Other System (Minor Head), 07-Grants for Extra Mural Research Projects through Research Institute (Pvt./Semi-Govt./University/NGO's etc.), 070031-Grants-in-aid (General) during 2020-21.

Yours faithfully,


(K.B. Sinha)

Under Secretary to the Govt. of India

Copy to: -

1. The Superintendent, P.D.E.A's Ayurved Rugnalaya & Sterling Multispeciality Hospital, Sector-27, Nigadi, Pune-411044 (Email- carchospital@gmail.com).
2. The DG, CCRAS, 61-65, Institutional Area, Opp. D Block, Janakpuri-110058.
3. Director (P&E), M/o AYUSH.
4. Budget/Cash Section, M/o AYUSH.
5. UC Folder.

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Principal

College of Ayurved And Research Centre
Akurdi, Pune - 411 044



F. No. S.14011/9/2020-Scheme (EMR)
Government of India
Ministry of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homeopathy

Plate-A, 2nd Floor,
Office Block-III, NBCC Complex,
East Kidwai Nagar, ND-23

Dated: 17th August, 2020

To

The Pay & Accounts Officer (Sectt.),
Ministry of Health & Family Welfare,
Nirman Bhawan, New Delhi.

Sub: - Release of Grants-in-aid of Rs.6,75,000/- as 1st installment for SARS CoV-2 infection and COVID 19 disease under Modified Extra Mural Research (EMR) Scheme during 2020-21-reg.

Sir,

In exercise to powers delegated under DFPR-1978, I am directed to convey the sanction of the President of India for release of an amount of Rs.6,75,000/- (Rupees Six Lakhs Seventy-Five Thousand Only) to "P.D.E.A's Ayurveda Rugnalaya and Sterling Multispecialty Hospital, Pune" as 1st installment of recurring grants for the Research Project titled "Randomized comparative clinical trial to assess the efficacy of Pippali Rasayana and Nagaradi Kashaya Ghana Vati combination as an adjuvant treatment with ICMR directed therapy in Covid-19 positive mildly symptomatic cases" under EMR Scheme during the year 2020-21.

2. The Sanction has been issued as per Rules 228 to 245 of General Financial Rules – 2017. The grant-in-aid will be subject to the conditions and provisions of the modified EMR Scheme for SARS CoV-2 infection and COVID 19 disease and no amount or part thereof shall be delivered/utilized to any other purpose than the one for which it has been sanctioned.
3. The accounts of the grantee institution/organization shall be open to inspection by the sanctioning authority and audit both by the CAG of India under the provisions of CAG (DPC) Act, 197: and internal audit wing of the O/o CCA of the Ministry, whenever the institution or organization is called upon to do so.
4. The Grants-in-aid of Rs.6,75,000/- (Rupees Six Lakhs Seventy-Five Thousand Only) is a recurring grants.
5. This sanction is subject to condition that the grantee institute will disburse this grant-in-aid through EAT (Expenditure, Advance and Transfer) Module of PFMS as per the guidelines under Ministry of Finance.
6. The sanction is issued subject to conditions that information/details in respect of Direct Benefit Transfer (DBT) under the budget heads Salary/Manpower and TA/DA as per notification of the Scheme under Section 7/57 of Aadhaar Act 2016 will be provided/uploaded to this Ministry on monthly basis as per DBT App/Format by the Principal Investigator/Organization.
7. The expenditure is debitable to the Demand No. 4- Ministry of AYUSH, 2210-Medical and Public Health (Major Head), 2200-Other System (Minor Head), 07-Grants for Extra Mural Research Project through Research Institute (Pvt./Semi-Govt./University/NGO's etc.), 070031-Grants-in-aid (General) during 2020-21. Scheme Code (3121-EMR).
8. No Utilization Certificate is pending against this institute during previous years under this scheme

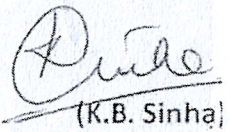
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KUNDAN B. SINHA
Under Secretary
Ministry of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homeopathy, Government of India
New Delhi

9. This issues with the approval of the IFD concurrence Dy. No. C-186 dated 10.08.2020.

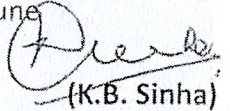
Yours faithfully


(K.B. Sinha)

Under Secretary to the Govt. of India

Copy forwarded for information and necessary action to:

1. The Director General of Audit, Central Revenues, I.P. Estate, New Delhi-110002
2. Niti Aayog, (Health Division), Sansad Marg, New Delhi.
3. SO (IFD-AYUSH), M/o H&FW, Nirman Bhavan New Delhi.
4. Cash (AYUSH) Section for preparing bill.
5. DDG (P&E), Ministry of AYUSH, New Delhi.
6. Sanction Register.
7. The P.D.E.A's Ayurveda Rugnalaya and Sterling Multispecialty Hospital, Pune - with the request that the above released grants should mandatorily be disbursed only through EAT (Expenditure Advance and Transfer) Module of PFMS as per the guidelines under Ministry of Finance.
8. Dr. Medha M Joshi Professor and HOD, Kayachikitsa, MD Kayachikitsa, P.D.E.A.'S, Ayurved Rugnalaya and Sterling Multispecialty Hospital, Sector 27, Nigdi Pradhikaran, Pune


(K.B. Sinha)

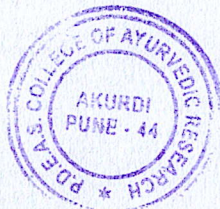
Under Secretary to the Govt. of India

N.B.

The Institute will submit/maintain the following documents in connection with the above grants: -

1. Utilization Certificate as per the provision of Scheme Guidelines & as per prescribed format of GFR-2017 (i.e. GFR-12A).
2. Audited Statement of Expenditure indicating accrued interest, if any, on the released grants.
3. Detailed Research Project Report against the released grants.
4. The Head of the Institute shall be personally accountable for proper utilization of the grants.
5. The grant is being released as 1st installment for the Research Project titled "Randomized comparative clinical trial to assess the efficacy of Pippali Rasayana and Nagaradi Kashaya Ghrita Vati combination as an adjuvant treatment with ICMR directed therapy in Covid-19 positive mildly symptomatic cases.
6. The details of approved budget for the above project are as under: -

Heads	Total	1st installment	10 % withheld amount
Ayurvedic Drug Authentication, Preparation Standardization & Packaging	Rs.50,000/-	Rs.50,000/-	-
Investigations: Nasopharyngeal /Throat Swab for RT-PCR for SARS-CoV-	Rs.3,50,000/-	Rs.3,20,000/-	30,000/-
CBC, CRP, RFT, BSLF&PP, ECG, CXR, HbA1C	Rs.2,00,000/-	Rs.1,75,000/-	25,000/-
Statistical Analysis/Support	Rs.10,000/-	-	10,000/-
Stationary	Rs.20,000/-	15,000/-	5,000/-
Contingency	Rs.20,000/-	15,000/-	5,000/-
PPE	Rs.1,00,000/-	Rs.1,00,000/-	-
Total	Rs.7,50,000/-	Rs.6,75,000/-	Rs.75,000/-



RECEIVED
Cash Section
Dated 17/8/20



Welcome:
 User Type:
AGENCYADM
 Agency: **PDEA's**
Ayurveda
Rugnalaya and
Sterling
Multispecialty
Hospital
 Financial Year:
2020-2021



[MHPU00024543]
 Logout
 Change Password

Public Financial Management System-PFMS

O/o Controller General of Accounts, Ministry of Finance

(formerly CPSMS)

AdhocReports

BharatKosh Reports

Home

E-Payment

Health Module

Agency

Reports

My Details

Masters

My Schemes

Agencies

EAT MIS Process

My Funds

Transfers

Advances

Scheme Allocation

Expenditures

Bank

Register/ Track Issue

Misc. Deduction Filing

Utilisation Certificate

Accounting System Integration

Bank Printing Templates

Manage Funds From Central Government

FinancialYear : 2020-2021

Schemes : * 3121 - Extra Mural Research Projects through Research

Bank Account : * 3279492107 - AYURVED RUGNALAYA AND STERLING

Status : Released

Search

Sanction Number	Scheme	Received Date	Received Amount	Status	Sanction File
S. 14011/9/2020- Scheme (EMR)	3121 - Extra Mural Research Projects through Research Institutes etc.	19/08/2020	675000.00	Released	



ANNEXURE - 5

Format for Annual Statement of Accounts to accompany request for release of next installment

(Year means Financial Year i.e. 1st April 2020 to 31st March 2021 of next year)

1. Sanction letter no. : F.NO.S.14011/9/2020-Scheme (EMR)
2. Total Project Cost : Rs 7,50,000/-
3. Sanction /Revised Project cost (if applicable) : Rs 6,75,000/-
4. Date of Commencement of Project : 17th Nov. 2020
5. Statement of Expenditure

S.No.	Sanctioned /Heads	Funds Allocated	Expenditure Incurred			Balance as on (Date)	Requirement of Funds up to 31 st March	Remarks
			1 st year	2 nd Year	3 rd Year			
1	Ayurvedic Drug Authentication, Preparation Standardization & Packaging	50,000/-	47,907/-			2,093/-		
2	Investigations : Nasopharyngeal/ Throat swab for RT-PCR for SARS-CoV-	3,20,000/-	1,36,200/-			1,83,800/-		
3	CBC, CRP, RFT, BSLF&PP, ECG, CXR, HbA1C	1,75,000/-	1,98,090/-				23,090/-	
4	Statistical Analysis/Support		10,000/-				10,000/-	
5	Stationary	15,000/-	14,800/-			200/-		
6	Contingency	15,000/-	12,470/-			2,530/-		
7	PPE	1,00,000/-	95,429/-			4,571/-		
10	Total	6,75,000/-	5,14,896/-			1,93,194/-	33,090/-	

Signature of Investigator Investigator: Kavyarhikar Investigator: Dr. Ravi Prasad Date: 17/11/2020	Signature of Head of Institution Superintendent Ayurvedic Hospital, Pimpri Date: 27/11/2020	Signature of Authorized Auditor with date & Seal Date: 27/11/2020
---	--	---

UCCV:-21135 279 0040 BG, 6457



TRUE COPY

Principal
College of Ayurved And Research Centre
Akurdi, Pune - 411 624

ANNEXURE-6

Check list for covering note to accompany Utilization Certificate of grant for the project for the period ending Aug 2020-Dec 2020

- 1) Title of the project : "Randomized comparative clinical trial to assess the efficacy of Pippali Rasayana and Nagaradi Kashaya Ghana Vati combination as an adjuvant treatment with ICMR directed therapy in Covid-19 positive mildly symptomatic cases"
- 2) Name of the institutions: PDEA's Ayurved Rugmalaya and Sterling Multispeciality Hospital, Nigdi, Pune - 411 044.
- 3) Principal Investigator : Dr. Medha M. Joshi
- 4) Ministry of AYUSH letter No. and date sanctioning the project.: F.No.5 14011/9/2020-Scheme(EMR)
- 5) Head of account as given in the original sanction letter :

Heads	Total	1 st Installment	10% withheld amount
Ayurvedic Drug Authentication, Preparation Standardization & Packaging	50,000/-	50,000/-	-
Investigations : Nasopharyngeal/ Throat swab for RT-PCR for SARS-CoV-19	3,50,000/-	3,20,000/-	30,000/-
CBC, CRP, RFT, BSLF&PP, ECG, CXR, HbA1C	2,00,000/-	1,75,000/-	25,000/-
Statistical Analysis/Support	10,000/-	-	10,000/-
Stationary	20,000/-	15,000/-	5,000/-
Contingency	20,000/-	15,000/-	5,000/-
PPF	1,00,000/-	1,00,000/-	-
Total	7,50,000/-	6,75,000/-	75,000/-

- 6) Amount received during the financial year (Please give No. and date of Ministry's sanction letter for the amount) : F.No.5 14011/9/2020-Scheme(EMR)
- 7) Total amount that was available for expenditure (excluding commitments) during the financial year (including amount remaining from earlier installment) : Rs. 6,75,000/-
- 8) Actual expenditure (excluding commitments) incurred during the financial year (up to 31st March) : Rs. 5,14,896/-
- 9) Balance amount available at the end of the financial year. : Rs. 1,60,104/-
- 10) Amount already committed, if any.: Rs. 7,50,000/-



GFR 12 - A
[(See Rule 238 (1))]

ANNEXURE-7

FORM OF UTILIZATION CERTIFICATE
FOR AUTONOMOUS BODIES OF THE GRANTEE ORGANIZATION

UTILIZATION CERTIFICATE FOR THE YEAR 2020-21 in respect
of recurring/non-recurring
GRANTS-IN-AID/SALARIES/CREATION OF CAPITAL ASSETS

1. Name of the Scheme : Extra Mural Research (EMR) Scheme
2. Whether recurring or non-recurring grants : Non Recurring
3. Grants position at the beginning of the Financial year.
 - (i) Cash in Hand/Bank : 0.00
 - (ii) Unadjusted advances 0.00
 - (iii) Total : 0.00
4. Details of grants received, expenditure incurred and closing balances: (Actuals)

Unspent Balances of Grants received years (figure as at Sl. No. 3 (iii))	Interest Earned There on	Interest deposited back to the Govern- ment	Grant received during the year			Total Available funds (1+2- 3+4)	Expenditure Incurred	Closing Balances (5-6)
1	2	3	4			5	6	7
			Sanction No.	Date	Amount			
0.00	0.00	0.00	P.No.5 B8011/9/2020 Scheme(EMR)	17/08/2020	5,75,000/-	5,75,000/-	5,14,896/-	1,60,104/-

Component wise utilization of grants

Grant-in-aid- General	Grant-in-aid- Salary	Grant-in-aid- creation of capital assets	Total
5,14,896/-	-	-	5,14,896/-

Details of grants position at the end of the year

- (i) Cash in Hand/Bank : 1,60,104.00
- (ii) Unadjusted Advances : 0.00
- (iii) Total : 1,60,104.00



Certified that I have satisfied myself that the conditions on which grants were sanctioned have been duly fulfilled/are being fulfilled and that I have exercised following checks to see that the money has been actually utilized for the purpose for which it was sanctioned:

- (i) The main accounts and other subsidiary accounts and registers (including assets registers) are maintained as prescribed in the relevant Act/Rules/Standing instructions (mention the Act/Rules) and have been duly audited by designated auditors. The figures depicted above tally with the audited figures mentioned in financial statements/accounts.
- (ii) There exist inter-l controls for safeguarding public funds/assets, watching outcomes and achievements of physical targets against the financial inputs, ensuring quality in asset creation etc. & the periodic evaluation of inter-l controls is exercised to ensure their effectiveness.
- (iii) To the best of our knowledge and belief, no transactions have been entered that are in violation of relevant Act/Rules/standing instructions and scheme guidelines.
- (iv) The responsibilities among the key functionaries for execution of the scheme have been assigned in clear terms and are not general in nature.
- (v) The benefits were extended to the intended beneficiaries and only such areas/districts were covered where the scheme was intended to operate.
- (vi) The expenditure on various components of the scheme was in the proportions authorized as per the scheme guidelines and terms and conditions of the grants-in-aid.
- (vii) It has been ensured that the physical and financial performance under Extra Mural Research (EMR) Scheme (name of the scheme has been according to the requirements, as prescribed in the guidelines issued by Govt. of India and the performance/targets achieved statement for the year to which the utilization of the fund resulted in outcomes given at Annexure - I duly enclosed.
- (viii) The utilization of the fund resulted in outcomes given at Annexure - II duly enclosed (to be formulated by the Ministry/Department concerned as per their requirements/specifications.)
- (ix) Details of various schemes executed by the agency through grants-in-aid received from the same Ministry or from other Ministries is enclosed at Annexure -II (to be formulated by the Ministry/Department concerned as per their requirements/specifications).

Date: 16th Mar. 2021

Place: Nigdi, Pune.

Signature

Name: Mrs. Vandana R. Patil

Chief Finance Officer

Organization (Head of the Finance)

(Strike out inapplicable terms)

Signature

Name: - Dr. Mrs. Ragini Rajan Patil

Superintendent

Ayurved Rajtalaj & Shiksha Mahasochity Hospital
Sec. 27, Nigdi, Pashchim, Pune - 44



ANNEXURE -10

FORMAT FOR FINAL STATEMENT OF EXPENDITURE

(To accompany the Final Report)

(To be submitted in original)

- 1) Sanction letter No. IF.NO.5.14011/9/2020-Scheme(EMR)
- 2) Total project cost : 7,50,000/-
(Sanctioned/revised project cost, if applicable)
- 3) Date of commencement of project : 17th Nov. 2020
- 4) Date of completion of project : 26th Mar.2021
- 5) Grant received in each year (financial):
 1st Instalment: Date of release of grant 19/08/2020 grant received Rs.6,75,000/-
 2nd Instalment: Date of release of grant - grant received Rs -
 3rd Instalment : Date of release of grant - grant received Rs -

Statement of Expenditure:

S.No	Sanctioned/Heads (Mention all items under each head)	Funds Allocated	Expenditure Incurred: Financial Year wise					Balance as on (Date)	Remarks
			1 st Instt.	2 nd Instt.	3 rd Instt.	Remainin g amount (10%)	Withheld Amount (10%)		
1	Ayurvedic Drug Authentication, Preparation Standardization & Packaging	50,000/-	50,000/-						
2	Investigations : Nasopharyngeal/ Throat swab for RT- PCR for SARS-CoV-19	3,50,000/-	3,20,000/-				30,000/-		
3	CBC, CRP, RFT, BSLF&PP, ECG, CXR, HbA1C	2,00,000/-	1,75,000/-				25,000/-		
4	Statistical Analysis/Support	10,000/-					10,000/-		
5	Stationary	20,000/-	15,000/-				5,000/-		
6	Contingency	20,000/-	15,000/-				5,000/-		
7	PPE	1,00,000/-	1,00,000/-				Nil		
8	Total	7,50,000/-	6,75,000/-				75,000/-		

Amount to be refunded/reimbursed (whichever is appropriate): Rs.1,50,000/- S K Y & CO

Signature of Principal Investigator: *[Signature]* with date & Seal
 Signature of Head of Institution: *[Signature]* with date & Seal
 Signature of Authorized Auditor: *[Signature]* with date & Seal
 Chartered Accountant: *[Signature]*
 Sec. 27, Nigdi, Pradhikaran, Pune - 44
 PIN - 2113527980086657



FORM GFR 12 A

UC ID: 18237474

FORM GFR 12-A
[See Rule 238(1)]

Form of Utilization Certificate FOR AUTONOMOUS BODIES OF THE GRANTEE ORGANIZATION

UTILIZATION CERTIFICATE FOR THE YEAR 2020-2021 in respect
of Recurring/non-recurring
GRANTS-IN-AID/SALARIES/CREATION OF CAPITAL ASSETS

1. Name of the Scheme : Extra Mural Research Projects through Research Institutes etc.-3121

2. Whether recurring or non-recurring grants : N/A

3. Grants positions of the beginning of the Financial year :

- (i.) Cash in Hand/Bank : 0.00
(ii.) Unadjusted advances : 0.00
(iii.) Total: 0.00

4. Details of grants received, expenditure incurred and closing balances: (Actuals) :

Unspent Balances of Grants received yrs(1)	Interest Earned there On(2)	Interest deposited back to the Government(3)	Sanction Number	Sanction Date	Amount(Rs) (4)	Total Available funds(5)= (1+2+3+4)	Expenditure Incurred(6)	Closing Balances(7)
0.00	0.00	0.00	S. 14011/9/2020- Scheme (EMR)	17-08- 2020	675000.00	675000.00	514896.00	160104.00

Grant-in-aid-General	Grant-in-aid-Salary	Grant-in-aid-creation of capital assets	Total
514896.00	0.00	0.00	514896.00

Details of grants position of the end of the year

3. Grants positions of the End of the Financial year :

- (i.) Cash in Hand/Bank : 160104.00
(ii.) Unadjusted advances : 0.00
(iii.) Total : 160104.00

Certified that I have satisfied myself that the condition on which the grants-in-aid was sanctioned have been duly fulfilled/are being fulfilled and that I have exercised the following checks to see that the money was actually utilized for the purpose for which it was sanctioned.

1. The main accounts and other subsidiary accounts and registers(including assets registers) are maintained as prescribed in the relevant Act/Rules/Standing instructions (mention the Act/Rules) and have been duly audited by designated auditors.
The figures depicted above tally with the audited figures mentioned in financial statements/accounts.

2. There exist internal controls for safeguarding public funds/assets , watching outcomes and achievements against physical targets against the financial inputs,ensuring quality in asset creation etc. & the periodic evaluation internal controls is exercised to ensure their effectiveness.

3. To the best of our knowledge and belief , no transactions have been entered that are in violation of relevant Act/Rules/Standing instructions and scheme guidelines.



4. The responsibilities among the key functionaries for execution of the schema have been assigned in clear terms and are not general in nature.

5. The benefits were extended to the intended beneficiaries and only such areas/districts were guidelines and terms and conditions of the grants-in-aid.

6. It has been ensured that the physical and financial performance under Extra Mural Research Projects through Research Institutes etc.-3121 (name of the scheme has been according to the requirements, as prescribed in the guidelines issued by Govt. of India and the performance/targets achieved statement for the year to which the utilization of the fund resulted in outcomes given at Annexure-1 duly enclosed.

7. The utilization of the fund resulted in outcomes given at Annexure-2 duly enclosed (to be formulated by the Ministry/Department concerned as per their requirements/specifications.)

8. Details of various schemes executed by the agency through grants-in-aid received from the some Ministry or from other Ministries is enclosed at Annexure-2 (to be formulated by the Ministry/Departments concerned as per their requirements/specifications).

Date: 26th May, 2021

Place: Nigdi, Pune.

Signature: *[Signature]*

Name: Ms. Vandana R. Pawar.

Chief Finance Officer
(Head of the Finance)

Signature: *[Signature]*

Name: Dr. Mrs. Rajini Rajan Patil

Head of the Organisation
Superintendent

Ayurved Rugmalaya & Sterling Multispeciality Hospital

Soc. 27, Nigdi, Pradhikaran, Pune - 44
(Strike out in inapplicable terms)





INSTITUTIONAL ETHICS COMMITTEE-II

Pune District Education Association's,

College of Ayurved & Research Centre

Sector No. 25, Pradhikaran, Nigdi, Pune – 411044

COMMUNICATION OF DECISION OF THE INSTITUTIONAL ETHICS COMMITTEE (IEC-II)

Department : -Agadtantra

Title of the study : "A Randomized Multi-Center, Prospective, Comparative Clinical Study to evaluate efficacy and safety of AP/VJT/SBO Ayurvedic Hair Oil in mild to moderate Hair loss in females."

Protocol No: AP/VJT/SBO/01/2022, Version no. 2.0 Dated 13th May 2022

Investigators Name : Dr.J.J.Phadke, Dr.Y.R.Kulkarni

Revised Review

Date of Review :17/05/22

Date of previous review, if revised application: 18/4/22

Name of the Reviewers :

Sr.No.	Designation	Name
1.	Nominated Chairman	Dr.Ajit Kolatkar
2.	Member Secretary	Dr.Yogita Jamdade
3.	Alternate Member Secretary	Dr.Dinesh Naik
4.	Basic Medical scientists	Dr. Meenal Lad
5.	Clinicians	Dr.Medha Joshi
6.	Legal Expert	Mrs.Pratibha Dalal
7.	Lay Person	Mr.Sanjiv Alurkar

Decision of the Ethics Committee:

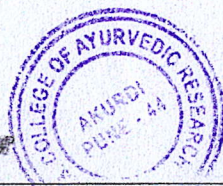
Recommended

Please note

- Inform IEC-II immediately in case of any Adverse Events and Serious Adverse Events
- Inform IEC-II in case of any change of study procedure, site and investigator
- The study must be conducted as per approved protocol. Any amendments in the Protocol/ICF/CRF must be approved from IIEC-II before implementation
- Members of IEC-II have right to monitor the trial with prior intimation
- The status of the study (Completed/Ongoing/Terminated) should be reported time to time.
- It is mandatory to obtain renewal of approval and apply for the same at the end of 24 months if required.
- The renewal of approval is subjected to submission of annual report. If the above application is not renewed within specified period, then the permission to renew the project may lapse.

(Signature)
(Member Secretary)
Dr. Yogita Jamdade

Member Secretary IEC - II
College of Ayurved & Research Centre
Akurdi, Pune - 411044



(Signature)
(Nominated Chairperson)
TRUE COPY
Principal

College of Ayurved And Research Centre
Akurdi, Pune - 411 044

MOU- AP/VJT/SBO/01/2022 Study.
(TIMER-PDEACARC)

THIS AGREEMENT is made and executed on 12th March 2022_ at Mumbai/Pune, by and between the following Parties:

Target Institute of Medical Education & Research (TIMER), a company in corporate and registered under Companies Act, 1956, and having its registered office at A wing 402-A/B/C, Jaswanti Allied Business centre, Ramchandra Lane Extension, Off link Road, Kachpada, Malad West, Mumbai-400064, Phone-022 62363654

Pune Office No.203, 2ndFloor, Jaymala Business Court, Besides Satyam Prima, Takle Nagar Manjri BK. Hadapsar Pune-411028 Phone:- 20-48562948 (herein after referred to as "TIMER"), which expression shall unless repugnant to the context or meaning thereof shall mean and include its successors in interest and assigns of the ONE PART.

AND

Pune District Education Association Pune, College Of Ayurveda & Research Center Sector No. 25, Pradhikaran, Nigdi, Pune-411 044 (hereinafter referred to "PDEACARC") which expression shall unless repugnant to the context or meaning thereof shall mean and include its successors in interest and assigns of the OTHER PART.

This agreement is executed for Clinical Trial Study "*A Randomized, Multi-center, Prospective, Comparative Clinical Study to evaluate efficacy and safety of AP/VJT/SBO Ayurvedic Hair Oil in mild to moderate Hair loss in females.*" Clinical Study, Protocol No. AP/VJT/SBO/01/2022, Version no. 1.0 Dated 26th Feb 2022.

Now, whereas M/s. AYURVED PRATISTHAN. have entrusted the work of conducting clinical trials on of AP/VJT/SBO Ayurvedic Hair Oil study to M/s. Target Institute of Medical Education and Research Pvt. Ltd., Mumbai/Pune and as whereas 'TIMER' has approached and discussed with 'PDEACARC' to undertake the clinical trials as referred above as per Protocol No. AP/VJT/SBO/01/2022, Version no. 1.0 Dated 26th Feb 2022. Now the terms of this M.O.U. witness as under –

Confidential



Page 1 of 11

MOU- AP/VJT/SBO/01/2022 Study.
(TIMER-PDEACARC)

1. The Objectives of the study shall be –

The objective of the study is to evaluate the efficacy and safety of AP/VJT/SBO Ayurvedic Hair Oil in mild to moderate Hair loss in females.

2. Study outcomes of the study shall be -

1. Primary Outcome:

- a. Comparative assessment of hair fall in AP/VJT/SBO Ayurvedic hair oil by running finger test over a period of 60 days.
- b. Comparative assessment of hair breakage in AP/VJT/SBO Ayurvedic hair oil by comb test over a period of 60 days.

2. Secondary outcomes:

- a. Comparative assessment of hair fall in AP/VJT/SBO Ayurvedic hair oil by Hair Pull test over a period of 60 days
- b. Comparative assessment of hair growth in AP/VJT/SBO Ayurvedic hair oil by comparing against standard infrequent hair oil users
- c. Comparative assessment of effect of AP/VJT/SBO Ayurvedic hair oil on dandruff in females by standard dandruff evaluation cards
- d. Comparative assessment of effect of AP/VJT/SBO Ayurvedic hair oil on quality of hair based on subject questionnaire including effect on graying, hair growth and hair density.
- e. Global assessment of overall change in hair loss by the physician
- f. Global assessment of overall change in hair loss by the subject
- g. Assessment of safety by observing episodes, severity and duration of any allergic reactions and adverse events

Safety Assessment Parameters:

- a. Tolerability of study treatments by assessing ADRs on study completion.
- b. Vital signs including allergic reactions, skin infections etc.
- c. Assessment of Overall Safety and Tolerability of the product by the physician and subject on global assessment scale by the investigator and by subject herself.

3. Study Design-

A Randomized, Multi-center, Prospective, Comparative Clinical Study.



4. The criteria for inclusion of subjects for this study shall be -

Subjects meeting all of the following criteria will be included in the study-

1. Female subjects between the age group of 18- 45 years both inclusive
2. Subjects suffering from mild to moderate hair loss (40-140 Hair by Comb test and Finger Test).
3. Subjects who are infrequent hair oil users
4. Subjects who are willing to give informed consent and ready to comply with the protocol
5. Subjects who are ready to provide regular follow ups till the completion of the Study.

5. Subject Exclusion Criteria

Subjects meeting any of the following criteria will be excluded from the study-

1. Subjects with severe Hair fall due to any clinically significant disorder/s like anemia, thyroid disorders etc.
 2. Subject with severe dermatological disorders of the scalp that might interfere with the study evaluation
 3. Subjects with recent disease history like, malaria, typhoid, jaundice and scalp diseases and subjects who in the opinion of the investigator are not eligible for enrollment in the clinical study
 4. Subjects who have regularly used anti-hair fall treatment with hair oils over the last 6 months.
 5. Subjects who have previously undergone hair transplantation procedures
 6. Subjects on systemic steroids for more than 14 days within 2 months prior to enrollment.
 7. Subjects on immunosuppressive drugs
 8. Known cases of Hypersensitivity to hair oil contents
 9. Subjects who have participated in any other clinical study since last 3 months
 10. Subjects who are reported pregnant/planning a pregnancy or lactating.
 11. Menopausal Women
6. AP/VJT/SBO Ayurvedic Hair Oil mainly contains the extracts of Ficus bengalensis Aerial root (Jata). It is very effective in hair fall control, strengthens hair roots and enhances hair growth..



7. After getting clearance from the Ethical Committee for this clinical study, the subjects attending the O.P.D. at 'PDEACARC' at Nigadi, Pune meeting inclusion criteria and voluntarily written consents, will be recruited for the study at O.P.D. basis. Patients (subjects) will be selected on screening visit and written informed consent will be taken from subjects for their participation in the study.

8. Treatment Plan:

Exposure to Investigational product shall be given to only those subjects who meet the inclusion/exclusion criteria. All screened subjects shall be entered into the screening log. Subjects who meet the inclusion/exclusion criteria shall be recruited in the study.

Recruited subjects shall be allotted a unique subject number and the number shall be entered in the enrolment log. If a subject drops out of the study after allocation of the unique subject number, that number shall not be re-allocated to another subject.

The time and date of recruitment shall also be recorded in the enrolment log. The time between recruitment and dispensing of the drug should be as short as possible.

If a subject drops out of the study after allocation of the unique subject number, that number shall not be re-allocated to another subject.

9. Treatment period

Female subjects will be advised to massage with approximately 10 ml of hair oil minimum three times a week for 60 days.

10. Rescue Medication

An accurate record of used rescue medications will be kept in the CRF. No other hair oil or shampoo will be permitted for hair fall control or dandruff control.

11. Diet /Activity/Other

All the subjects will be advised to continue their regular diet and exercise regimen (which they are already following) during the entire study.



12. Follow Up

Safety information shall be collected at each study visit. Subjects with SAEs or AEs that are ongoing at the end of the study treatment shall be followed until the resolution of the event.

13. Description of Investigational Product

The investigational instrument manufactured is already approved by the FDA.

14. Procedures to be performed daily during study treatment

After Ethics committee's clearance for the clinical study and subsequent registration of clinical trial at CTRI website, subjects attending OPD meeting inclusion criteria and ready to provide written informed consent for participation in the study, will be recruited in the study. The treatment will be given on OPD basis. 20 subjects with in mild to moderate Hair loss in females will be screened for eligibility criteria to get 20 evaluable cases at the end of the study.

On screening visit, written informed consent will be obtained from the subjects for their participation in the study. Subject's history will be recorded and her physical examination will be done. Assessment of inclusion and exclusion criteria will be done. Assessment of hair loss will be done and those subjects having mild to moderate hair loss (40-140 Hair by Comb test, Running Finger Test) will be included in the study. Subjects will also be assessed based on hair pull test. Subject's dandruff score will be evaluated on standard dandruff evaluation strip. Subject's clinical examination will be done and past history of any illness or medicines will be recorded. Subjects will undergo lab examinations like Hb% and TSH. Subjects with low Hb% and thyroid disorders will be excluded from the study. If Subjects are eligible, then they will be enrolled in the study. Subjects will be advised not to take any medication for the treatment of Hair loss except the study medication during the study period. Subjects will be advised to continue their usual routine diet and exercise/activity regimen, which they are already following, during the entire study period. Subjects will be advised to come to the hospital/site for the baseline visit within 5 days after the screening visit.

On baseline visit (Day 0), the subject will be recruited in the study if she meets all the inclusion criteria As per computer generated randomization list, subject will be randomized to one of the study groups. There will be two groups, one group of participants will be provided with



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AP/VJT/SBO Ayurvedic Hair Oil while the other will be assigned to the group who are infrequent hair oil users. Investigational Product dispensing will be done to Subject's in the AP/VJT/SBO Ayurvedic hair oil group. Subject will be asked to do a Running Finger Test (RFT) and Comb Test (CT) in the presence of the investigator and hair will be collected and counted in a labelled poly bag and documented in the CRF.

Hair pull test will be done in which subjects small section of hair (approximately 20-60 hair) from the proximal portion of the scalp will be grasped between the thumb, index and middle fingers from the base of the hairs near the scalp and firmly, but not forcefully, tugged away from the scalp. The number of hairs pulled away from scalp will be counted and recorded in CRF. Average length of hair from the Pull test will be measured and recorded in CRF. Subject's dandruff score will be evaluated on standard dandruff evaluation strip. Clinical examinations, both General and Hair Specific will be done. Subjects will be assigned to either any of two groups based on computer generated randomization list and the hair oil bottle will be dispensed. Subjects will be advised to massage with approximately 10 ml hair oil on the scalp with fingertips before going to bed in night or before bath for minimum 3 times a week. Subjects will be asked to do hair wash thrice a week. On every follow up visit except last follow up visit, subjects from the AP/VJT/SBO Ayurvedic hair oil group will be provided with the hair oil. On every follow up visit, the empty container will be collected from the subjects in the AP/VJT/SBO Ayurvedic hair oil and drug compliance will be checked.

Subjects will be called to the investigators site on day 15, 30, 45 for follow up. At every follow up visit subject's clinical examination will be done. Subjects will be asked for any adverse event during this period. Assessment of Hair loss will be done by Running Finger Test (RFT), Comb Test (CT) and Hair pull test in the presence of investigator. Subject's dandruff score will be done on dandruff evaluation strip. Average hair length will be recorded on each follow-up visit. Average length of hair from the Pull test will be measured and recorded in CRF. On every visit subjects will be interrogated based on questionnaire to evaluate their quality of hair (both on graded scale and VAS) including effect on dandruff, graying and hair growth.



On day 60 i.e., end of treatment visit, clinical examinations will be done. Subjects will be asked for any adverse event during this period. Assessment of Hair loss will be done by Running Finger Test (RFT), Comb Test (CT) and hair pull test in the presence of investigator.

Subject's dandruff score will be done on dandruff evaluation strip. Average hair length from the Pull test will be recorded. Subject's will be interrogated based on questionnaire to evaluate their quality of hair (both on graded scale and VAS) including effect on dandruff, graying and hair growth. Global evaluation based on the subject and the investigator will be done at the final visit. Subjects will be advised to stop Study medication and take advice of investigator for further treatment.

If the subject had AE/SAE, the details of the incidence will be documented in the source document and CRF. SAE, if any, will be reported to the IEC in a SAE reporting form. Rescue medication used, if any, will be recorded in the CRF.

All the subjects will be asked to take the advice of the investigator for further treatment at end of Study.

15. ASSESSMENT OF SAFETY

A. Specifications of Safety Variables

Safety shall be assessed by clinical review of all safety parameters, including the following:

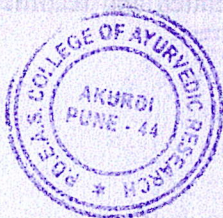
- a. Adverse event reporting
- b. Vital signs including pulse rate, respiratory rate, body temperature, and blood pressure.

Safety variables shall be listed individually for detailed clinical review when needed.

The changes from baseline in vital signs shall be presented descriptively by treatment (formulation). Additional tables shall summarize adverse events by severity and relationship to study product as well as leading to SAEs and withdrawal of the subjects from the study.

16. ETHICAL CONSIDERATIONS & REGISTRATION OF STUDY:

The study will be conducted, recorded and reported strictly in accordance with ICH GCP guidelines laid down for Pharmaceutical drugs and Medical Devices and the ICMR ethical guidelines for biomedical research on human participant's amendment in 2006, which are originated from WMA-Declaration of Helsinki.



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During the conduct of the clinical study, rights, safety, and wellbeing of the study participants will be given prime importance.

Good laboratory practices (GLP) will be followed for all the Laboratory investigations to be performed under the study. The instrument will be manufactured with compliance to Good Manufacturing Practices (GMP) as applicable for electronic products in India.

17. Ethics Committee review and communications

The study protocol and related documents will be submitted to the Ethics committee of the respective study center for review and approval. Subjects will not be recruited to the study until the IEC approves the study. Any changes in this study plan or protocol will be implemented only after they are reviewed and approved by the IEC. IEC will keep its close watch on the study conduct for the entire study duration.

For any IEC related query or complaints, a person from the ethics committee, to be approached, is chairman/secretary of the respective Ethics committee.

18. Written Informed consent process

On screening visit, voluntary written informed consent, for their participation in the study, will be obtained from the subjects on ICF; printed in the language best understood by them. During the Informed consent process, subjects will be explained the objectives of the study, design of the study and possible risks and benefits of participation in the study. They will be given enough time to ask questions to fully understand the study. If the subject is illiterate, informed consent process will be in presence of an impartial witness, if the subject agrees to participate in the study, his/her thumb impression will be taken on the ICF and also the signature (with date) of impartial witness will be obtained on the same ICF. One copy of the ICF will be handed over to the subject. The informed consent process will be documented

19. Subject confidentiality statement

The identity of the study subjects will not be provided to any party except study related personnel, Sponsor or their representatives, ethics committee and representatives of Government regulatory bodies. The data generated and recorded from the study will be kept

Confidential



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confidential and in a coded form. The recorded data, after analysis, may be published by the sponsor or with the investigator's consent in peer-reviewed scientific journals without revealing the identity of any subject.

20. Subject Insurance Policy

The Sponsor undertakes to bear any compensation and cost for medical treatment of any possible trial-related injuries to the study subjects, caused specifically due to the use of the investigational product. The investigator shall be completely indemnified by the Sponsor in this regard. All subjects will be compensated for the expenses arising for medical/surgical treatment for specifically any Adverse Reaction related to the study drug. All participating subjects in the study will be covered under the Clinical trial liability insurance.

21. CTRI registration:

The study will be registered with the Clinical Trial Registry of India after approval from at least one of the IEC. The status of other EC approval will be updated accordingly.

22. Appointment of Research Coordinator:

The Investigator or Institute shall appoint and entrust the study work to at least one research Coordinator. TIMER will make payments to the Research Coordinator for the clinical study as per mutually agreed terms.

22. Payments:

'TIMER' shall pay to MAMSGAK as per the agreed Budget of the study. **Service Tax or TDS or any other taxes will be applicable as per the rules.** Payment schedule will be follow

Milestone	Payment
Milestone 1- Advance	IEC Fee along with submission of Document
Milestone 2- Site Initiation Visit	10% of total budget (Less IEC Fee) at the time of initiation of the clinical study.
Milestone 2- Screening Visit	25% of total budget (Less IEC Fee) upon recruitment of 18 patients.
Milestone 4- Study Completer	25% of total budget (Less IEC Fee) upon recruitment of 36 patients.
Milestone 5- Study Completion	Balance 10% of total budget (Less IEC Fee) upon completion of the study follow up visits
Milestone 6- Report Submission	Final 15% at the time of submission of Clinical study report



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(Payment agreed is exclusive of GST or TDS or any other taxes which will be added to the budget).

23. Judistraction:

In case of any dispute not settled by mutual discussions, Pune shall be the area of Judistraction.

24. Conduct of Clinical Study:

The clinical study under this protocol will be done as per the current ICH-GCP guidelines for conducting clinical studies. The clinical study will be carried out as per the protocol agreed upon.

25. Documentation & Communications:

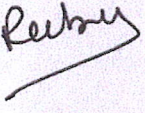
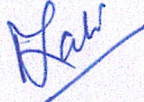
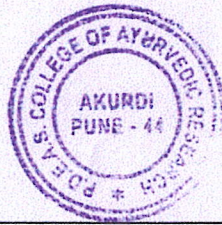
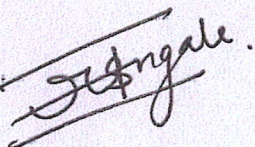
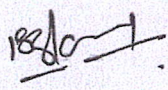
Investigator will periodically communicate the process of the clinical trial to the CRO.
Investigator will cooperate during the monitoring visits by providing all the relevant details.
Maintaining the source documents and records for the relevant period of time (5 Years) will be done at the Site.

26. Publications, IPR:

Any intellectual knowledge generated through the study shall belong to the sponsor and the investigator and organization shall not have any rights on it. Nothing related to the clinical study or the product shall be revealed to the press or any other organization/persons without the consent of the sponsor. The rights to publish the data will lie with the sponsor, however, no data or publication will be done without the prior information and approval of the Investigator. The Investigators involved in the study will be the Authors of the Publication whenever it is done.



This M.O.U. has been signed by the parties at Mumbai on this 12th day of March 2022.

Signed for and on behalf of, Target Institute of Medical Education and Research Pvt Ltd., Pune Office No.203, 2 nd Floor, Jaymala Business Court, Besides Satyam Prima, Takle Nagar Manjri BK. Hadapsar Pune-411028 Phone:- 20-48562948	Signed for and on behalf of, Pune District Education Association Pune , College Of Ayurveda & Research Center Sector No. 25, Pradhikaran, Nigdi, Pune-411 044
Authorized Signatory : 	Authorized Signatory : 
Name: Dr. Ruby Dubey	Name: Dr. Ragini Patel Principal P.D.E.A.S College of Ayurved And Research Centre Nigdi, Pune - 411 044.
Title: Manager-Clinical Trial Operation Target Institute of Medical Education & Research Pvt. Ltd	Title: 
Company Stamp:	Company Stamp:
Witness:	Witness:
Name: Aditya Sushil Ingale 	Name: Dr. Bobade R. B. 
Signature:	Signature:

Vatajatadi Study Tentative Budget

DATE: 04/03/2022

STUDY TITLE: A Randomized, Multi-center, Prospective, Comparative Clinical Study to evaluate efficacy and safety of Vatajatadi Ayurvedic Hair Oil in mild to moderate Hair loss in females

SAMPLE SIZE: 20 completed patients

STUDY DURATION: 3 month

SPONSOR NAME: Welex Laboratories Pvt . Ltd.

Sr. No.	Particulars	Amount (Rs.)
1	IEC Fees	10000
2	PI Fees	15000
3	Co-Investigator	15000
4	CRC	10000
4	Lab Investigation	At Actual
5	Institutional Charges (10 % of Total Budget)	-
6	Total	

Payment schedule:

- IEC fee will be paid at the time of submission of documents
- 25% charges of PI Fees and Co-investigator fees will be paid after enrolment of 25% subjects.
- 25% charges of PI Fees and Co-investigator fees will be paid after enrolment of 50% subjects.
- 25% charges of PI Fees and Co-investigator fees will be paid after enrolment of 75% subjects.
- Remaining 25% charges of PI Fees and Co-investigator fees will be paid after singing of final report
- Charges for contingencies will be done as and when necessary
- A independent CRC will be appointed from Target Institute and will be paid on monthly basis
- Institutional charges will be paid at the end of the trial.
- All applicable taxes will be deducted while making payments to the respective individual/Institute.
- All investigators and Co investigators names to be added in publication of the study.

For,

Ruby

Target Institute of Medical Education and Research,
Mumbai



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[Signature]
Principal

College of Ayurved And Research Centre
Akurdi, Pune - 411 044

Vatajatadi Study Tentative Budget

ANNEXURE - I

INVESTIGATIONS

Sr. No.	Investigations	Charges (Rs.)	Frequency	No. of Patients	Total
1	Hb%		1	15	
2	TSH		1	15	



Target Institute of Medical
Education & Research Pvt. Ltd.

Registered & Corporate Office(Mumbai):
A-402 A/B/C, Jaswanti Allied Business Centre,
Ramchandra Lane Extension, Kachpada,
Off Link Road, Malad West, Mumbai – 400064.
Phone: 022 62363654

Registered & Corporate Office (Pune):
Office No. E-203, Second floor, Jaymala Business
Court, Besides Satyam Prima, Takle Nagar, Manjri bk.
Hadapsar, Pune- 412307.
Phone: 020 48562948

Date 21/03/2022

To,
The Member of Secretary
Institutional Ethics Committee
Pune District Education Association Pune,
College Of Ayurveda & Research Center
Sector No. 25, Pradhikaran, Nigdi, 411044

Sub: .Submission of Clinical Study Documents to Institutional Ethics Committee of Pune District
Education Association Pune, College Of Ayurveda & Research Center. for review and approval

Respected ,

As discussed, please find enclosed following documents for clinical study titled “A Randomized, Multi-center, Prospective, Comparative Clinical Study to evaluate efficacy and safety of AP/VJT/SBO Ayurvedic Hair Oil in mild to moderate Hair loss in females.” please find enclosed documents for review and Approval.

Sr.No	Document	Version No.& Date
1	Clinical Study Protocol	Version no. 1.0 Dated 26th Feb 2022
2	Case Report Form	Version no. 1.0 Dated 26th Feb 2022
3	Informed Consent Form English	Version no. 1.0 Dated 26th Feb 2022
4	Informed Consent Form Marathi	Version no. 1.0 Dated 26th Feb 2022
5	Informed Consent Form Hindi	Version no. 1.0 Dated 26th Feb 2022
6	Informed Consent Form Translation certificate (, Marathi & Hindi)	Version no. 1.0 Dated 26th Feb 2022
7	SAE Reporting Form	Version no. 1.0 Dated 26th Feb 2022
8	Investigator Undertaking	-
9	CV (PI & Co-I)	-

10 COA OF IP

Thanks & Regards,
For

Target Institute of Medical Education and Research Pvt Ltd
Dr. Ruby Dubey
Manager-Clinical Trial Operation

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Principal

College of Ayurved And Research Centre
Akurdi, Pune - 411 044

Received
21/03/22
28/3/22



www.targetinstitute.in info@targetinstitute.in



Target Institute of Medical
Education & Research Pvt.Ltd.

Registered & Corporate Office(Mumbai):
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Hadapsar, Pune- 412307.
Phone: 020 48562948

Date: - 15/04/2023

Revised Budget for Hair Oil Study Akurdi Hospital Pune

(Version 1.0, 15th Apr 2023)

CRO: - Target Institute of Medical education & Research Pvt Ltd 402 Awing A/B/C Jaswanti Allied Business Centre Ramchandra lane Ext kachpada Malad W	SITE: - Ayurved Rugnalaya & Sterling Multispeciality Hospital Pune	
Contact Person: -Dr Ruby Dubey Email Id: - drrubytargetinst@gmail.com Phone No: -8975533215	PI Name: - Email Id: - Phone No: -	
STUDY TITLE: “A Randomized, Multi-center, Prospective, Comparative Clinical Study to evaluate efficacy and safety of AP/VJT/SBO Ayurvedic Hair Oil in mild to moderate Hair loss in females.”		
PROTOCOL NO: AP/VJT/SBO/01/2022, Version no. 1.0 Dated 26th Feb 2022		
SAMPLE SIZE: 20 Completed patients		
STUDY DURATION: 3 months		
SPONSOR NAME: AYURVED PRATISTHAN.		
Sr No	Head	Amount in Rs.
1	IEC Fees	10000.00
2	Principal Investigator Charges	15000.00
3	Co-Investigator Charges	15000.00
4	CRC	10000.00
5	Lab Charges (At Actual)	9600.00
6	Total	59600.00
7	Institutional Charges (10 % of Total Budget)	5960.00
8	Grand Total	65560.00

Payment schedule:

- IEC fee will be paid at the time of submission of documents
- 25% charges of PI Fees and Co-investigator fees will be paid after enrolment of 25% subjects.
- 25% charges of PI Fees and Co-investigator fees will be paid after enrolment of 50% subjects.
- 25% charges of PI Fees and Co-investigator fees will be paid after enrolment of 75% subjects.
- Remaining 25% charges of PI Fees and Co-investigator fees will be paid after singing of final report
- Charges for contingencies will be done as and when necessary
- Institutional charges will be paid at the end of the trial.
- All applicable taxes will be deducted while making payments to the respective individual/Institute.
- All investigators and Co investigators names to be added in publication of the Study



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Akurdi, Pune - 411 044

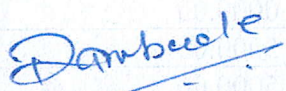
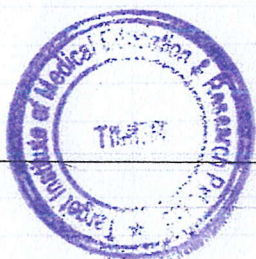
www.targetinstitute.in

info@targetinstitute.in

ANNEXURE – I

INVESTIGATIONS

Sr. No.	Investigations	Charges (Rs.)	Frequency	No. of Patients	Total
1	Hb% (If Require)	250	1	24	6000.00
2	TSH (If Require)	150	1	24	3600.00
Total Amt-----					9600.00

CRO	SITE
For, Target Institute of Medical Education & Research Pvt Ltd	For, Ayurved Rugnalaya & Sterling Multispeciality Hospital Pune
 	



Target Institute of Medical
Education & Research

Registered & Corporate Office :
A-402 A/B/C, Jaswanti Allied Business Centre,
Ramchandra Lane Extension, Kachpada,
Off Link Road, Malad West, Mumbai - 400064
Phone : 022 62363654

To,
Ayurved Rugnalaya & Sterling
Multispeciality Hospital Akurdi Pune.

Date: 25/04/2023

Sub: Final Payments for Clinical studies on Hair Oil Study.

Dear Dr,

Please find along with this letter towards payments for the above-mentioned clinical studies. These payments are as per your mail (copies attached) and are the Final Payment for these studies. Please note that we have deducted a TDS of 2% on each payment. TDS certificate will be provided to you accordingly.

Sr. No	Study Product	Chq. Amount Rs. And Chq. No	TDS deducted	Total Amt
1.	Hair Oil Study	Rs.54,447/- Chq No.001480 Dated 24/04/2023 ICICI BANK	Rs.1,113.00	Rs.55,560.00
Total Paid Amt-----				54,447.00

Kindly acknowledge the receipt of the same.

Many thanks

For, *Dambee*
Target Institute of Medical Education & Research Pvt Ltd
Mumbai



Name: -	Ayurved Rugnalaya & Sterling Multispeciality Hospital
Account No: -	3279492107
Bank Name: -	Central Bank of India



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Principal

College of Ayurved And Research Centre
Akurdi, Pune - 411 044

CLINICAL STUDY PROTOCOL

"A Randomized, Single blind, Multi-center, Prospective, Comparative Clinical Study to evaluate efficacy and safety of Four Hair Oil formulations in mild to moderate Hair loss in females."

Protocol No: HO/EM/2017, Version 1.0, Dated 14th June 2017

The confidential information in the following document is provided to you as an investigator, coordinator and /or applicable institutional review board /ethics committee. By accepting this document, you agree that the information contained herein shall not be disclosed to others, without written authorization from Target Institute of Medical Education & Research (TIMER) and Sponsor Emami Ltd except to the extent necessary to obtain informed consent from those persons to whom the study medications shall be administered or for regulatory purposes when asked by authorized regulatory personnel.

