Bharati Vidyapeeth Deemed University
Interactive Research School for Health Affairs (IRSHA)
Annual Report July 2023- June 2024

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Overview of Director

It is my privilege to present the Annual report of Interactive Research School for Health Affairs (IRSHA) for the year 2023-2024. All the departments of IRSHA were successful in receiving financial support of Rs.1179.71 Lakhs from national funding agencies for carrying out their research work. This year student fellowships of Rs. 19.09 lakhs were received. In the current year 3 students were awarded PhD degree.

In the year 2023-2024, the external funding through consultancy projects at NIBEC crossed 1000 lakhs. The efforts taken at NIBEC for testing of samples from SARS-CoV-2 clinical trials for determining neutralizing antibody titer were recognized by Dr Jitendra Singh, Minister Incharge Science & Technology, Government of India.

In the year 2023-2024 research work at the institute culminated into 28 publications research articles and 3 book chapters

Several activities had been organized at the institute and also the staff and students participated in national and international events. A brief summary of these events, activities and achievements by all the staff members has been presented in the current report.

I appreciate the support and hard work of all the scientists, technical and administrative staff for their commendable performance.

Finally I sincerely thank the management for extending all the support for undertaking our research work.

Dr A C Mishra, M Sc, Ph D, LL B, FASc, FNA
Director

Name of the Programme: Mother and Child Health

1. Title: Building evidence and designing solutions to prevent stillbirths in India – a collaborative approach to retrospectively analyze pregnancycohorts in India (Project ID: MCH/24/1/E) Multicentric Project; Funding: ICMR; Sanctioned Amount: Total Sanctioned Rs. 8,05,917/-; Duration: Feb 2024 to Aug 2024; Investigator at IRSHA: Dr. Sadhana Joshi; Human Ethical Approval: -N/A

Background: Stillbirths pose a significant yet overlooked challengein India, with an estimated rate of 14 per 1000 live deliveries. Despite India being responsible for the highest number of stillbirths globally, there has been a recent commitment to reduce stillbirth and early neonatal mortality rates to single digits by 2030. The rarity of stillbirth outcomes, coupled with diverse definitions, has hindered comprehensive research and solution development. To overcome this, a collaborative effort is proposed, leveraging existing high-quality pregnancy cohorts in India.

Novelty: The proposed initiative is novel in its collaborative approach, bringing together diverse pregnancy cohorts to create a harmonized and integrated database. This collaboration aims to redefine stillbirth outcomes, identify risk factors, and develop a risk stratification framework. The study's uniqueness lies in its use of advanced statistical and machine learning models for predicting stillbirth risk, ultimately contributing to the global commitment to ending preventable stillbirths.

Work done: Objectives: Harmonized Database Creation: Identify prospective pregnancy cohorts. Harmonize variables and develop a common data dictionary. Integrate data into a common database.

Data Analysis: Estimate region-specific trends in stillbirth rates. Identify modifiable risk factors. Develop and internally validate a risk stratification framework using clinical, ultrasound, and biological predictors.

Objective 1: Form a core committee with technical and statistical representation from each cohort. Weekly meetings to harmonize variables and report progress monthly.

Objective 2: Descriptive statistics for demographic and baseline characteristics. Stillbirth rates presented regionally and over time. Univariate and multivariable analyses to identify and adjust for risk factors. Development of a clinical prediction model using advanced statistical and machine learning models. Internal validation through k-fold cross-validation. Assessment of model performance using R2, calibration, discrimination, PPV, NPV, ROCcurve, and AUC.

Results and Conclusion: The collaborative effort is expected to yield: Comprehensive region-specific stillbirth rate estimates. Identification of modifiable riskfactors. A validated risk stratification framework for pregnant women. Insights into clinical, ultrasound, and biological predictors of stillbirth. A decision support tool for clinicians to assess stillbirth risk. In conclusion,

this initiative strives to bridge the knowledge gap surrounding stillbirths in India by pooling resources, standardizing data, and applying advanced analytical methods, ultimately contributing to the global goal of ending preventable

2. Title: Exploring the role of maternal fatty acids, placental fatty acid metabolism, and inflammation in determining infant health in gestational diabetes mellitus (Project ID: MCH/22/2/E) Multicentric Project; Funding: DBT; Sanctioned Amount: Total Sanctioned Rs. 9551840/-; Duration: Feb 2022 to Feb 2025; Investigator at IRSHA: Dr. Sadhana Joshi; Human Ethical Approval: IEC/2021/71

Background: Gestational diabetes mellitus (GDM), affects 1 in 7 pregnancies. It has short and long-term consequences for mother and child. However, the mechanisms contributing to the pathophysiology are unclear. Alterations in maternal dietary patterns may result in a chronic inflammatory state associated with GDM. Omega-3 and omega-6 fatty acids are precursors for specialized pro-resolving mediators that exhibit anti-inflammatory and proresolving mechanisms thereby regulating inflammation. Impaired production of eicosanoids leads to excess activation or quenching of inflammation which may resultin GDM.

This study will utilize the samples biobanked under the REVAMP study. The REVAMP study has recruited women in early pregnancy and followed them until delivery. We will follow children to examine anthropometric measures, blood pressure and neurodevelopmental outcomes. We have a unique opportunity to examine early pregnancy and placental fatty acid andinflammatory markers with childhood outcomes

Work done: The current study has used samples which have been collected from GDM and non GDM women under the ICMR CAR project. This study utilizes maternal blood samples collected in early pregnancy and placentae at delivery of women who later developed GDM. An additional Ethics approval for the current study has been given by the Bharati Vidyapeeth Medical College Institutional Ethics Committee.The current study utilized the samples which have been collected from GDM (n=209) and non GDM (n=207) women under the ICMR CAR project.

The following activities are undertaken:

- Standardization of questionnaires for cognitive performance.
- Maternal erythrocyte fatty acid analysis
- Homogenization of placental samples on non-GDM and GDM samples.
- Total protein estimation from tissue lysates.
- Standardization of protein levels of placental inflammatory markers.
- Standardization of anthropometric measures and questionnaires for cognitive performance completed.
- Anthropometry, Cognitive performance and blood pressure in children has been initiated.

Results and Conclusion: Women with GDM had higher maternal age ($p<0.01$), systolic BP and diastolic BP ($p<0.05$ for all) at delivery. The OGCT values were significantly higher ($p<0.01$) in GDM women as compared to non-GDM women. Trimmed placental weight was higher and baby length was lower ($p<.0.01$ for both) in women who developed GDM as compared to non-GDM.

The current study reports increased saturated fatty acids, increased omega-3 fatty acids (ALA and EPA) and reduced LA and AA levels in the women who developed GDM before the clinical diagnosis of GDM. These altered fatty acid levels could be attributed to changes in the fatty acid metabolism enzymes such as desaturases and elongases. Further, we have observed lower LA, AA, EPA,DHA, Omega-6 fatty acids and total PUFA and higher SFA levels in the cord blood of women who developed GDM indicating disturbed placental transport of these fatty acids towards the fetus. Levels of fatty acid metabolism enzymes and transporters will be estimated in the next year. Fatty acids like AA and DHA play a major role in cognitive development of the infant. Lower levels of AA and DHA in the cord blood of GDM women may possible have implications for impaired cognition in their children.

Long chain polyunsaturated fatty acid (LCPUFA) are precursors for the biosynthesis of a variety of mediators known as specialized pro-resolving mediators (SPMs) that play a crucial role in regulating inflammation. There is limited data on the levels of inflammatory cytokines in the placentae of women with GDM. Our data indicates increased inflammatory cytokines (TNF-alpha, NFkappa Band Interleukin 10) in the placentae of women with GDM. Further analysis on pro-resolving mediators like resolvins, protectins and lipoxins will help to understand the role of early maternal fatty acids status on placental inflammation and its influence on the pathophysiology of GDM.

3.Title: Understanding the association and underlying molecular mechanisms of early life 'Double-burden' of malnutrition and non-communicable disease risk in adolescence (Project ID: MCH/23/3/E) Multicentric Project; Funding: DBT; Sanctioned Amount: Total Sanctioned Rs. 158,95,630/-; Duration: Oct 2023 to Oct 2026; Investigator at IRSHA: Dr. Sadhana Joshi; Human Ethical Approval: IEC/2022/107

Background: Research by our collaborative group has shown that part of the increased non-communicable disease (NCD) risk in Indians comes from changes in fetal body composition. The undernourished Indian newborn is typically light and thin (average birth weight 2.7kg) and has a low lean body mass but is disproportionately adipose (the 'thin-fat' Indian). This phenotype persists through childhood and into adult life, and is associated with increased cardiometabolic risk at relatively low levels of obesity. The effects of early life undernutrition are exacerbated by poor weight gain in infancy and rapid childhood weight gain even in the absence of overt obesity.

Our past research in this area, the resources we have developed, and our network of wide-ranging expertise, place us in a unique position to take this field forward in India. Within our group, we

possess expertise in in various disciplines including nutrition, public health, longitudinal cohort studies, and mechanistic research (including genetics, epigenetics, transcriptomics and associated technical platforms), exemplifying the necessary multi-disciplinary strengths to conduct this study and derive meaningful conclusions with translational potential.

We will investigate the mechanism through which early life nutritional status and life style factors (diet and physical activity) target various molecular pathways associated with cardiometabolic status and cognitive performance in 3-7 years old children and in adolescence. Further, as an additional strength of this cohort, we will investigate the complex interplay between maternal nutrition and above mentioned factors and its influence on cardiometabolic disease risk.

Identifying these interactions will help to devise a strategy to reduce the problem of double burden of malnutrition (features of under- and over-nutrition) and future NCD risk.

Work done: In the current proposal we will investigate the mechanism through which early life nutritional status and lifestyle factors (diet and physical activity) target various molecular pathways associated with cardiometabolic status and cognitive performance in 3-7 years old children and in adolescence. This study will utilize the IRSHA-BVDU cohort where pregnant women and their newborn were recruited at delivery in Bharati Hospital, Pune (n= 681 mother-child pairs). Identifying these interactions will help to devise a strategy to reduce the problem of double burden of malnutrition (features of under- and over-nutrition) and future NCD risk. Maternal and cord blood samples from all mother-child pairs are available stored at appropriate temperature. The children were followed up at 3-7 years and detailed nutritional data, physical activity, anthropometry, blood pressure and cognitive performance were recorded. We are now following up these children who are at their adolescence age.

Results and Conclusion:

- Mothers delivering SGA babies had lower BMI and higher SBP and DBP as compared to mothers delivering AGA babies.
- Children born SGA had lower BMI at 3-7 years and continued to lower in the adolescent age. In contrast sum of skinfolds were lower at 3-7 years and similar at adolescent age.
- SGA children at adolescent age had higher triglyceride and VLDL levels
- RDW-CV count was higher in adolescents born SGA at birth.
- Maternal dal/pulsed, ghee and butter consumption was positively associated with weight and height of children at 3-7 years
- Maternal ghee and butter consumption was positively associated with BMI and skinfolds of children at 3-7 years
- Maternal consumption of milk products, ghee/butter, and cereals positively associated with cognitive performance of children at 3-7 years
- Maternal erythrocyte omega-6 fatty acids and polyunsaturated fatty acids (PUFA) levels at delivery were lower whereas maternal erythrocyte saturated fatty acids were higher in mothers who delivered SGA babies as compared to those delivered AGA babies
- In contrast, cord erythrocyte omega-3 fatty acids and docosahexaenoic acid (DHA) levels were higher in the SGA babies as compared to AGA babies possibly due to

biomagnification.

- Fatty acids associated with anthropometric and cognitive measures of children at 3-7 years
- RNA sequencing was carried out with 23 samples to generate 60 million paired end reads that mapped efficiently to human reference database. Downstream analysis is ongoing.

4.Title: Early Interventions to Support Trajectories for Healthy Life in India (EINSTEIN). Healthy Life Trajectories Initiative (HeLTI) (Project ID: MCH/17/4/E) Multicentric Project; Funding: DBT; Sanctioned Amount: Total Sanctioned Rs. 743.44 Lakhs; IRSHA Share: Rs.13.50 Lakhs; Duration: Dec 2017 to Nov 2025; Investigator at IRSHA: Dr. Sadhana Joshi; Human Ethical Approval: IEC/2018/34

Background: The study is a community-based, cluster randomized intervention with three arms (pre-conception, pregnancy and control) set in rural Mysore, South India, with individual villages forming the basis for the cluster. The primary outcome at age 5 years in the children across all HeLTI cohorts is adiposity, measured by fat mass index. Other key outcomes at 5 years include; overweight and obesity, glucose metabolism, blood pressure, and infant/child development.

Work done: Formative work: Mysore Team commenced the formative work in November 2018 in three villages

Community engagement: Extensive community engagement to explain the study and assess the community's interest and willingness to not only participate, but also contribute to the study design and delivery

Qualitative work: Undertook focus group discussions (FGDs) with village women, husbands, mothers/mothers-in-law, village leaders and officials, and local community health staff.

Quantitative work: Analyses of fatty acids have been undertaken at IRSHA, Bharati Vidyapeeth, Pune.Plasma fatty acid profile revealed a high n6/n3 PUFA ratio (total n6=33.51 g/100g (SD 4.57); total n3=1.51 g/100g (SD 0.60); n6/n3 ratio=26:1

Intervention development: The core members of the India and Canada teams conceptualised the intervention modules and prepared the outline in February 2019. The intervention will be delivered across four phases. The local team then developed six pre-conceptional modules: General Health; Healthy Eating; Health Lifestyle; Keeping Clean; Positive Thinking; and Preparing for Pregnancy.

Harmonisation and governance : All four HeLTI teams have worked together to harmonise data variables and intervention domains and we have achieved a high degree of harmonisation

5. Title: Role of Maternal Nutrients and its influence on Inflammation and Angiogenesis in women with Gestational Diabetes Mellitus. (Project ID: MCH/23/1/P) Guide: Dr. Sadhana

Joshi; PhD Student: Shweta D. Madiwale; Ethical Approval: BVDUMC/IEC/84A, dated 20.04.2023

Background: The study explores the role of maternal supplementation of folate and vitamin B12 in women with GDM and Non-GDM and also observs the folate and vitamin B12 rich food intake longitudinally in GDM and Non-GDM women. The study also explores the levels of angiogenic markers that is VEGF (Vascular endothelial growth factor), PlGF (placental growth factor), Flt-1 (fms-like tyrosine kinase) in GDM and non-GDM women

Work done: Maternal supplementation of folate and vitamin B12 and dietary intake of folate and vitamin B12 rich food intake were estimated on 100 Non-Gestational Diabetes Mellitus women and 100 women with Gestational Diabetes Mellitus which were estimated at three different time points across gestation that is 11-13 weeks, 18-22 week and 26-28 weeks. The levels of the above mentioned placental angiogenic markers were also estimated on GDM and non-GDM women.

Results and Conclusion: This study includes 200 pregnant women (100 Non-GDM and 100 GDM women). GDM women had higher daily consumption of vitamin B12 rich foods at V1 and V3 as compared to non-GDM women. Whereas, the frequency of consumption of folate-rich foods was similar in the GDM and non-GDM groups at all time points. Also, the percentage of GDM women taking vitamin B12 supplements was higher at V1 and folate supplements was higher at V1 and V3 as compared to non-GDM women. Placental VEGF levels were similar among the groups whereas, placental PLGF and Flt-1 levels were significantly reduced in the GDM group compared to non GDM group.

6. Title: Placental fatty acid metabolites, oxidation and transport in Gestational Diabetes Mellitus. (Project ID: MCH/23/2/P) Guide: Dr. Sadhana Joshi; PhD Student: Nikita P. Joshi; Ethical Approval:

Background: The study explores the role of placental fatty acid specialized pro-resolving mediators, fatty acid oxidation markers and transporters in GDM and non-GDM women. The study also explores the association of these placental markers with cognitive performance in children born to these women.

Work done: Review of literature was completed. Title and objectives were approved by the Research Advisory Committee. Standardization and estimation of placental fatty acid specialized pro-resolving mediators (resolvins, protectins and lipoxins) has been completed. Standardization of markers involved in fatty acid oxidation (PPAR-α and CPT1A) has been completed. Assessment of cognitive performance in children has been initiated.

Results and Conclusion: This study includes 400 pregnant women (200 Non-GDM and 200 GDM women). Placental protein levels of RvE1, RvD1 and RvD2 were lower ($p<0.001$ for all) in GDM group as compared to non-GDM women.

7. Title: Fatty acid status in pregnancy and it's association with cardiometabolic risk variables in children . (Project ID: MCH/23/2/P) Guide: Dr. Sadhana Joshi; PhD Student: Ms. Vrushali Vilas Kadam;Ethical Approval: Not yet taken

Background: The study investigates maternal and cord fatty acid status in small for gestational age (SGA) and appropriate for gestational age (AGA) infants. It also explores the relationship between maternal and cord fatty acids and child growth parameters, as well as their impact on cardiometabolic risk.

Work done: Objectives were defined and research methodology was decided. Literature review on maternal fatty acid status and cardiometabolic risk in children. Compilation of data and analysis on maternal fatty acid status and cardiometabolic risk in children follow up, recruitments, blood and data collection of adolescents.

Results and Conclusion: This study included 671 mother-offspring dyads, categorized into two groups SGA (n=281) and AGA (n=390) at Bharati Hospital, Pune, India. Our results indicate that (1) mothers delivering SGA babies had lower plasma PUFA and higher MUFA levels (2) Conversely, cord plasma DHA and total n-3 fatty acids were higher in SGA group when compared to the AGA group (3) Maternal low PUFA and high MUFA levels were associated with an increased risk of SGA birth. (4) Sum of skinfolds measures was lower in SGA children (5) Higher maternal n6:n3 ratio was associated with increased BMI, and skinfold thickness in children. The study underscores the significance of maternal and cord fatty acid profiles in associating with early childhood health outcomes.

8. Title: Exploring the role of excess maternal vitamin B12 supplementation on cardiometabolic risk and cognitive function in the offspring. (Project ID: MCH/24/3/P) Guide: Dr. Sadhana Joshi; PhD Student: Sunaina Chhetri; Ethical Approval: BVDUMC/6174/2024/01/02, dated 27.02.2024

Background: Maternal nutrition, including vitamin B12 is vital for fetal growth and development. During pregnancy vitamin B12 is essential for the normal growth and development of the fetus (Finkelstein et al., 2015). Vitamin B12 and long-chain polyunsaturated fatty acids, are interlinked in the one-carbon cycle, which plays an important role in fetal 'programming' of adult diseases. Changes in developmental processes during pregnancy can increase disease risk later in life, known as the "Developmental Origins of Health and Disease" (DOHaD). Vitamin B12 is crucial

for pregnancy outcomes, with deficiencies linked to an adverse effect. However, less is known about effect of excess vitamin B12. This study reports the effect of prenatal supplementation of excess vitamin B12 on pregnancy outcome and fatty acids levels in Wistar rats.

Work done: Female rats were divided into three groups from pre-pregnancy to pregnancy, viz Control, Intermediate and Excess. The intermediate group and excess group were supplemented with 1.5 μg/day and 120 μg/day of vitamin B12 respectively. Dams were sacrificed at d20 of gestation to collect dam blood, brain, placenta, pup liver and pup brain. Fatty acids levels from dam erythrocytes was analysed using gas chromatograph.

Results: Vitamin B12 levels were significantly higher in excess group ($p<0.01$) as compared to intermediate and control group. Folate and homocysteine were found to be similar across groups. The weight gain across pregnancy was similar between groups. The dam brain weight in the excess group was lower ($p < 0.05$) as compared to the intermediate group. There was no difference in litter weight or litter size. Myristic acid (MYR) ($p<0.01$), stearic acid (STE) ($p<0.05$) and saturated fatty acids (SFA) ($p<0.05$) were higher in the excess group as compared to the control group. In contrast, total omega-6 fatty acids ($p<0.05$) and omega 6 to omega 3 ratio ($p=0.052$) were lower in the excess group as compared to the control group.

Conclusion: Our study demonstrates no adverse effect of excess maternal vitamin B12 supplementation on pregnancy outcome. Excess vitamin B12 showed differential effects on various fatty acids studied. Further studies need to examine the long term effects of excess vitamin B12 supplementation.

9. Title: Impact of Assisted Reproductive Technology (ART) on Placental Development and Birth Outcome. (Project ID: MCH/24/4/P); Guide: Dr. Deepali Sundrani; PhD Student:Aishwarya Uttam Kapare ;Ethical Approval:

Background: Assisted reproductive technology (ART) procedures such as in vitro fertilization (IVF) and intrauterine insemination (IUI) are used as infertility treatments. In India, the rate of infertility is on the rise thereby increasing the demand for these treatments. ART procedures are undertaken during gametogenesis and early embryo development. These are important stages where epigenetic modifications like DNA methylation are established for normal fetal development. ART procedures overlap with these stages, potentially affecting gene activity which may influence the development of the placenta and fetus. The study explores the influence of Assisted Reproductive Technology (ART) on placental development and birth outcome. This study examines the fatty acid composition in women who conceived through ART procedures and compared them with naturally conceived women (Non-ART).

Work done: Review of Literature was done for the particular topic. Title and objectives were finalised and approved by RAC committee. Estimated fatty acids from the placenta of women underwent ART and Non-ART women by using Gas Chromatography.

Results and Conclusion: This study includes 157 pregnant women (93 Non-ART and 64 ART women). We observed lower placental total omega-3 fatty acids ($p<0.05$) and omega-6:omega-3 PUFA ratio ($p<0.05$) was higher in ART group suggesting that imbalanced ratio of omega-6 to omega-3 that may promote an inflammatory environment thereby affecting birth outcome.

10. Title: Role of Fatty Acids and Neurotrophins in Influencing Cognitive Performance in Children Born to Mothers with Preeclampsia. (Project ID: MCH/24/5/P);Guide: Dr. Deepali Sundrani; PhD Student: Bhargavi A. Patel; Ethical Approval:

Background: The study explores the role of fatty acid and neurotrophins in adolescents born to mothers with preeclampsia and Non-preeclampsia and their association with cognitive performance. The study further examines gene expression and DNA methylation profile of placental neurotrophins and fatty acid desaturases and their association with cognitive performance in the adolescents.

Work done: Literature review was conducted concerning preeclampsia (PE) and factors associated to growth and development of adolescents born to mothers with preeclampsia.The title, objectives, study design, sample size, and methodology for the study was discussed and finalized. Based on the comments by the RAC members, the title of the study has been finalized to "Role of Fatty acids and Neurotrophins in Influencing Cognitive Performance in Children Born to Mothers with Preeclampsia." Recruitment of adolescents is being conducted. Data collection for the following components is ongoing :

- Clinical assessment
- Dietary patterns (24HR Recall and Food frequency Questionnaire)
- Cognitive Performance
- Blood collection for biochemistry

Results and Conclusion: A thorough literature review has been completed. Till July 2024, 150 children have been recruited and have been assessed for the above mentioned components. Blood processing for these samples have been simultaneously completed. Plasma , RBC, WBC and serum have been segregated and stored at -80degree celcius for further analysis.

Name of the Programme: Cancer Biology

1. **Title: Evaluating The Anti-Cancer Activity of Homoeopathic Medicine Copaiva Officinalis (Mother Tincture ,6c) On Pc3 Prostate Cancer Cell Line; Funding: BVDU Minor research Project ID: (CR/24/1/P)Duration: One year; Sanctioned Amount: 1.0 Lakh Investigators: PI - Dr. Aniket Mali Co PI- Dr. Monali Thopate Ph.D. Students: - Human Ethical Approval: NA**

Background: Homeopathy and other complementary therapies are often used to enhance cancer patients' quality of life and mitigate the side effects of conventional treatments. Homeopathy, which employs ultra-high diluted preparations, has shown potential in preclinical studies against prostate cancer cell lines, though limited research addresses its use for treating the disease itself. Over the past 20 years, studies have suggested homeopathic high dilutions may be beneficial in experimental cancer models. Prostate cancer is the most commonly diagnosed cancer worldwide and the sixth leading cause of cancer-related death in men. Diagnosis relies on biopsies, MRI scans, and PSA testing, though PSA screening remains controversial. New diagnostic tools, such as advanced PET scans, risk stratification bioassays, and germline testing, are now available.

Work done: The homeopathic medicine COPAIVA OFFICINALIS is used to evaluate its anti-cancer properties in the form of the mother tincture (MT) and its potency (6C) along with respective potentized DA as a control. First, the effect of MT and 6C were tested for cell cytotoxicity in 8 different concentrations using MTT assay. MT showed significant cell cytotoxicity at lower concentrations compared to 6C potency. Cell viability assay was performed using a Trypan dye exclusion assay. MT also reduced cell viability at same doses. Cell apoptosis was performed by JC-1 dye to evaluate the effectiveness of selected drugs as anti-cancer agent.

Results: The homeopathic medicine Copaiva Officinalis was evaluated for its anticancer properties in both mother tincture (MT) and 6C potency, using MTT and Trypan dye exclusion assays. MT showed significant cytotoxicity at lower concentrations compared to 6C potency in 8 different doses. The Trypan dye exclusion assay confirmed that MT also reduced cell viability at the same concentrations. Apoptosis was further assessed using the JC-1 dye, demonstrating that MT had a more pronounced effect on inducing apoptosis compared to the 6C potency. These findings suggest that Copaiva Officinalis MT may have potential as an anticancer agent.

Conclusion: Copaiva Officinalis mother tincture demonstrated significant anticancer potential by inducing cytotoxicity, reducing cell viability, and promoting apoptosis more effectively than its 6C potency.

2. **Title: Exploring the Therapeutic Potential of Enterolactone for Targeting Cancer Stem Cells and Metastasis in Triple Negative Breast Cancer; Project ID: (CR/24/2/P) Funding: NA; Duration: Five years Sanctioned Amount: NA Investigators: PI - Dr. Aniket Mali Co PI- NA Ph.D. Students: - Ms. Akanksha Mahajan Human Ethical Approval: NA**

Background: Triple-negative breast cancer (TNBC) is an aggressive subtype affecting younger, premenopausal women, with an incidence rate of up to 31% and a prevalence of about 25% in India. It has a poor prognosis, with high recurrence and a 5-year survival rate under 30% for metastatic cases, even with chemotherapy. TNBC's treatment challenges include chemoresistance, invasiveness, and relapse. A key focus in TNBC research is on cancer stem cells (CSCs), which drive tumor progression, metastasis, and treatment resistance. CSCs can self-renew, resist therapies, and facilitate tumor relapse. Combining conventional and CSC-targeted therapies is a promising strategy, potentially improving tumor eradication and reducing relapse by disrupting CSC signaling and drug resistance mechanisms.

Work done: This study explored Enterolactone's (EL) potential against TNBC, targeting CSCs and metastasis. A network pharmacology approach identified EL's therapeutic targets, followed by gene ontology, KEGG enrichment, molecular docking, and molecular dynamics simulations for key targets. GeneMANIA analysis expanded the target network. The role of EL against TGF-β effects on CSCs was investigated in MDA-MB-231 cells, assessing CSC subpopulations (CD44+/CD24-/low) and mammosphere size. Flow cytometry analyzed EL's impact on mitochondrial mass and apoptosis, and its effects on cytoskeletal remodeling (actin and tubulin) were studied.

Results: EL formed stable interactions with key targets like AKT1, GSK3B, IGF1R, and SRC, while EGFR and EZH2 showed higher fluctuations. GeneMANIA highlighted Wnt-βcatenin pathway involvement, with EL binding to newly identified targets. EL also showed antimetastatic potential through interactions with TGF-β/SMAD and Notch pathways. In vitro, EL reduced mammosphere size and CSC subpopulations in MDA-MB-231 cells, even with TGF-β. It countered TGF-β-induced mitochondrial changes and restored apoptosis sensitivity. EL also remodeled actin and tubulin structures, counteracting the TGF-β-driven CSC phenotype.

Conclusion: Enterolactone (EL) shows promise as a TNBC therapeutic, targeting CSCs and metastasis through key pathways like Wnt-βcatenin and TGF-β/SMAD. EL reduces CSC populations, counters TGF-β effects, and remodels cytoskeletal elements, making it a potential candidate for TNBC treatment.

3. **Title: Investigating the Therapeutic Potential of Plant Lignan for targeting Lipid Metabolism Reprogramming in Breast Cancer. Project ID: (CR/24/0/P) Funding: NA Duration: Five year Sanctioned Amount: NA Investigators: PI - Dr. Aniket Mali Co PI- NA Ph.D. Students: - Prajakta Patil; Human Ethical Approval: NA**

Background: Breast cancer remains the leading cause of cancer-related deaths among women globally [Globocan 2018]. Current treatment options are hindered by chemotherapy resistance [Yardley et al., 2013], partly due to dysregulated metabolic pathways such as de novo lipogenesis and cholesterol biosynthesis [Luo et al., 2017]. These pathways not only promote tumor progression and cell proliferation but also contribute to treatment resistance [Roberts et al., 2017]. Cancer cells, including those in breast cancer, rely heavily on de novo synthesis of fatty acids and cholesterol to support membrane formation and signaling, crucial for growth and survival [Zaidi et al., 2013; Huang and Freter, 2015]. Key proteins like HMGCR, SREBP-2, and LDLR mediate enhanced cholesterol biosynthesis, while enzymes such as FASN and ACC-1 are pivotal in de novo lipid biosynthesis [Gustbée et al., 2015; Vazquez-Martin et al., 2007; Chajes et al., 2006]. Targeting these pathways could offer new therapeutic avenues. Dietary lignans, known for their cholesterol and lipid regulatory properties in other diseases, have shown promising anticancer effects in breast cancer [Sun et al., 2017; Helli et al., 2016]. This study explores the anticancer potential of selected lignans by modulating de novo lipid and cholesterol metabolism in breast cancer cells.

Work done: An LMR model was developed in MDA-MB-231 cells using different glucose concentrations. SE's effects on gene expression were analyzed through qRT-PCR, and its influence on LMR-related cell migration, colony formation, and actin stress fiber formation was evaluated using wound healing, colony formation assays, and phalloidin staining, respectively. SE's impact on LMR-associated cancer stem cell (CSC) traits was also examined, including mammosphere formation, mitochondrial mass increase (mitotracker green), and apoptosis resistance (JC-1).

Results: For the in-vitro LMR model, MDA-MB-231 cells were treated with varying glucose concentrations: no glucose, 5.5mM (normal), and 15mM/25mM (high glucose). This led to LMR-associated cellular and molecular changes, including the upregulation of genes involved in fatty acid and cholesterol synthesis, cholesterol efflux, beta-oxidation, and fatty acid elongation, confirming LMR induction. The changes in EMT and CSC phenotypes were also observed. SE treatment reduced LMR-induced migration, colony formation, EMT markers (E-cadherin, vimentin, snail, etc.), actin stress fibers, and CSC traits like CD44 and Oct4 expression, mammosphere formation, mitochondrial mass, and induced apoptosis resistance in MDA-MB-231 cells.

Conclusion: The findings confirm that SE can effectively act against LMR in TNBC cells investigated via glucose-induced LMR in MDA-MB-231 cells to show its anticancer potential against TNBC. Further, SE also showed the effects on LMR-associated EMT and CSC processes confirming its ability to show anti-metastatic effect in LMR-associated metastatic behaviour of MDA-MB-231 cells

4. **Title: Exploring the therapeutic potential of Matairesinol in targeting metastasis in prostate cance Project ID: (CR/24/4/P) r. Funding: NA Duration: Five year Sanctioned Amount: NA Investigators: PI - Dr. Aniket Mali Co PI- NA Ph.D. Students: - Ms. Rama rajadnya Human Ethical Approval: NA**

Background: Prostate cancer is one of the threatening malignancies observed among men globally (GLOBOCAN,2018). Current treatment strategies i.e. androgen deprivation therapy for PCa lead to the progression of Hormone-resistant CRPC because of self-sufficiency of prostate tumor cells in androgen production (GLOBCAN, 2020). Therefore, preventing the transition to CRPC and treating CRPC effectively have become critical challenges for prostate cancer management.

Work done: Various assays were performed to analyze the effect of MAT **on** TGF-β-induced EMT in PC3 cells. The morphological changes were observed after TGF-β induction. The colony formation assay was performed to assess the ability of the single cell to grow into a colony. Further, the q-PCR was conducted to evaluate the effect of MAT on EMT-specific markers in PC3 cells after induction. Mitotracker dye was also used for mitochondrial dynamics analysis in cells.

Results: This study provides a detailed analysis of MAT's inhibitory effects on TGF-β-induced epithelial-mesenchymal transition (EMT) in PC3 prostate cancer cells. TGF-β triggered a morphological shift to a fusiform shape and promoted EMT, while MAT treatment effectively countered these changes by restoring cobblestone morphology, reducing cell viability, and inhibiting colony formation in a dose-dependent manner. MAT also reversed the loss of E-cadherin and downregulated mesenchymal markers like N-cadherin and vimentin. Additionally, MAT disrupted mitochondrial dynamics and metabolic reprogramming linked to EMT and reduced the tumor sphere formation ability, highlighting its potential as an anti-EMT agent in prostate cancer.

Conclusion: MAT effectively inhibits TGF-β-induced EMT in PC3 prostate cancer cells by restoring epithelial characteristics, disrupting mitochondrial dynamics, and reducing cancer stem cell-like properties.

Name of the Programme: Obesity- Diabetes

1. **Title: Elucidating mechanisms of anti-hyperglycemic activity of selected herbal formulations. Project ID: (ObDb/24/1/E) Funding: CCRAS, Ministry of Ayush; Duration: April 2024- March 2026; Sanctioned Amount: Rs. 53,96,148/-; Investigators PI: 1. Dr. Vidyashree Anchan*; 2. Dr. Supriya Bhalerao, Co- I: 1. Dr. S.H. Doddamani*: 2. Dr. Asavari Joshi#; Collaborating Institution: *Research Officer, Central Ayurveda Research Institute, Bengaluru Collaborating Department: #Assistant Professor, Centre for Innovation in Nutrition Health Disease.(CINHD), IRSHA, Bharati Vidyapeeth (Deemed to be) University, Pune**

   Background: Type 2 Diabetes mellitus (T2DM) is a complex multifactorial disorder characterized by hyperglycemia either due to the relative deficiency in insulin secretion or impaired action of insulin affecting glucose uptake. Although research on T2DM has culminated into development of various oral anti-diabetic agents, these drugs are not sufficient to establish glucose homeostasis. Further, they are associated with adverse effects of various degree prompting the search of alternate strategies involving the use of medicinal plants. Many herbal drugs and formulations have been tested for their anti-diabetic activity. However, for majority of the cases, the research remains restricted to evaluation of anti-hyperglycemic activity and is seldom extended to elucidation of the mechanism involved thereof. The selected herbal formulations, 2 shortlisted by CARI, Bengaluru and 2 by BVDU- IRSHA, whose anti-hyperglycemic activity has already been established using animal models, will be studied with respect to following mechanisms; Insulin sensitization, Insulin secretagogues, Alpha- Glucosidase inhibition, Sodium-glucose transport proteins-2 (SGLT2) inhibition, Dipeptidyl peptidase IV (DPP IV) inhibition, Glucagon-like peptide (GLP-1).

   Objectives:

   a) Primary: To establish mechanisms of anti-hyperglycemic activity of selected herbal formulations.
   b) Secondary: To evaluate the effect of herbal formulations on insulin sensitization in adipocytes, myocytes and hepatocytes.
      To evaluate the effect of herbal formulations on insulin secretion in pancreatic Beta cells.
      To evaluate α-glucosidase inhibitory and DPP- IV inhibitory activity (in vitro) of herbal formulations.

   The project has been sanctioned and funding has been received.
   The project will start from July, 2024.

2. **Title: Evaluation of Triphala as an Add-on Intervention for Sustained Weight Loss in Overweight and Obesity: A Randomized Placebo-Controlled Clinical Trial;**

(ObDb/24/2/E) Funding: ICMR- NITM; Duration: April 2024- March 2027; Sanctioned Amount : Rs. 6,69,720/- Investigators PI: Dr. Banappa Unger* Co-PI : Dr. Supriya Bhalerao; Collaborating Institution: Scientist 'E', Dept. of Pharmacology, ICMR- NITM (National Institute of Traditional Medicine), Belgavi

Background: Sustained weight loss is challenging in obesity. The reason for weight-regain is attributed to adaptive metabolic rate. The reduction in lean body mass (LBM), an unintended effect of current weight-loss programs, causes a drop in resting metabolic rate (RMR) and consequent renewed weight gain. Therefore, counteracting the drop in LBM and RMR is necessary for sustainable weight loss. Triphala is a preferred Ayurveda Rasayana for obesity management & claimed to benefit LBM building. Our preliminary work and published literature indicates the potential energy expenditure effect of Triphala. A systematic review of RCTs revealed that Triphala successfully reduces body weight and waist circumference, but its effect on RMR and sustained weight loss remains unknown. The proposed project thus focuses on evaluating potential of Triphala as an adjuvant therapy for sustained weight loss in overweight and obese individuals.

Objectives:

a) Primary: To determine the effectiveness of Triphala add-on intervention on sustainable weight loss in overweight and obese adults.
b) Secondary: To determine the effect of Triphala add-on intervention on lean body mass, resting metabolic rate, blood glucose, lipid profile, blood pressure and quality of life in overweight and obese adults.

The project has been sanctioned and funding is yet to be received.

3. **Title: Effect of Lipitaezar tablets, a proprietary formulation in patients suffering from Non-alcoholic fatty liver disease (NAFLD): an open label, randomized, controlled clinical study. Project ID (ObDb/23/3/E); Funding: Amardeep Pharma Pvt. Ltd. Duration:August 2023- May 2024; Sanctioned Amount:Rs. 5,41,266/-; Investigators: PI: Dr. Supriya Bhalerao Co-I:1. Dr. Dadasaheb Maindad*; 2. Dr. Priscilla Joshi# Collaborating Institution(s): *Associate Professor, Department of Medical Gastroenterology, Bharati Hospital & Research Centre, Bharati Vidyapeeth (Deemed to be) University, Pune $Professor and Head, Department of Radiodiagnosis, Bharati Hospital & Research Centre, Bharati Vidyapeeth (Deemed to be) University, Pune;** Project Staff:Dr. Revati Bhatt; Ethics Approval:BVDUMC/IEC/205 (23/08/2022); CTRI registration: CTRI/2023/06/054391

Background: Non-alcoholic fatty liver disease (NAFLD), a condition with excess accumulation of fat has been estimated to have its global prevalence between 25·2% and

29·8%, with a proportional rise along with the epidemics of obesity and type II diabetes. It encompasses a wide spectrum of histological and clinical manifestations, ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), with or without fibrosis that may develop into cirrhosis, hepatocellular carcinoma and liver failure. There are no known treatments available for NAFLD, however, clinical trials for the same showed a modest improvement in liver biochemistries and histology induced by vitamin E administration and thus is the preferred drug of choice, in most cases. Lipitaezar, a polyherbal formulation of Amardeep Pharma Pvt. Ltd. contains a range of herbal plants that have been researched individually for their effects on liver and shown some positive results in a small pilot study. This study has been proposed to evaluate the effect of Lipitaezar vs Vitamin E in individuals with NAFLD.

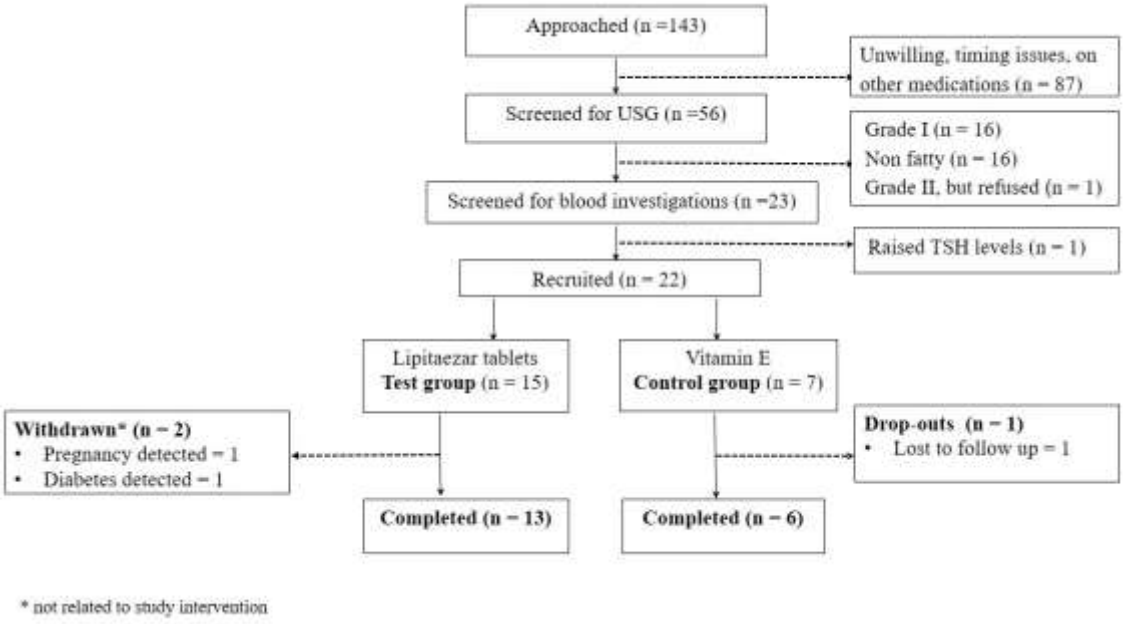
Objectives:

- To determine the effect of Lipitaezar tablets on fatty liver changes
- To evaluate the effect of Lipitaezar tablets on insulin resistance
- To assess the effect of Lipitaezar tablets on weight and waist circumferences
- To study the safety of Lipitaezar tablets

Work done: The study began post obtainment of Ethics approval (BVDUMC/IEC/205) and CTRI registration (CTRI/2023/06/054391). Individuals from the community were screened as per the eligibility criteria. The eligible individuals were randomised to two groups; Lipitaezar tablets or Vitamin E for a duration of 3 months.

Results: Of 143 approached individuals, 56 were screened for Ultrasonography of the Abdomen & Pelvis. Out of 23 eligible individuals, 22 were recruited and further, 19 participants completed the study; 13 from the Lipitaezar tablets group and 6 from the Vitamin E group. The participant flow is given below. (Figure 1)

Figure 1: Consort flow diagram



Steatosis, Liver stiffness & Fibrosis

A mild decrease in the mean UGAP scores, which denote steatosis, was seen in both the groups on day 90 compared to day 0, which was statistically significant ($p = 0.0263$) only in the Vitamin E group. In case of elastography, the extent of fibrosis and liver damage remained almost constant in the Lipitaezar group post treatment. Contrary to this, Vitamin E group showed increase in the median elastography score. Like UGAP, the Fib-4 score, which indicates advanced liver fibrosis, also showed a mild decrease in the Lipitaezar group while it remained constant in Vitamin E group. There was no significant difference between the two groups.(Figure 2 a, b, c)

Figure 2: Effect of Lipitaezar tablets on Steatosis, Liver stiffness & Fibrosis of liver

Figure 2a: Steatosis

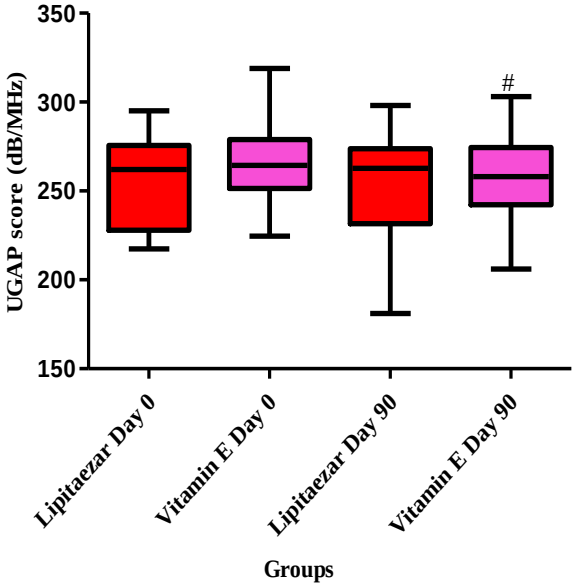


Figure 2b: Liver stiffness

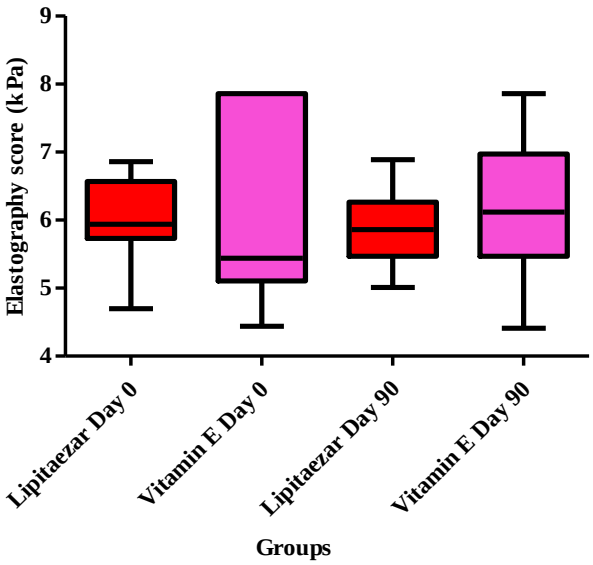
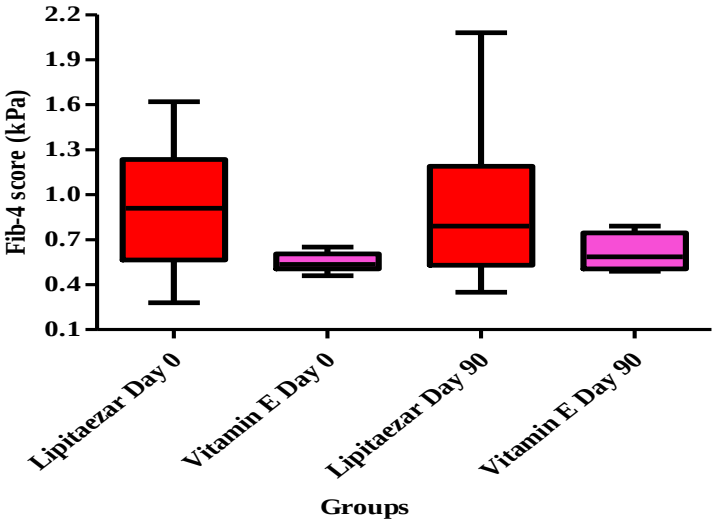


Figure 2c: Liver fibrosis



Glycemic and lipid profiles

Among these, Lipitaezar showed a mild decrease in insulin resistance as well as significant decrease in Glycosylated haemoglobin. Also, both groups showed a mild decrease in total cholesterol and Low density lipoprotein levels.

Conclusion: Lipitaezar effectively did not allow increase in steatosis, fibrosis and arrested further liver damage. It improved glycemic profile by causing decrease in the insulin resistance, as well as enhanced renal function. Almost all the parameters pertaining to safety profile of Lipitaezar were within normal range. Lipitaezar, thereby showed promising results to be considered as a potential and safe candidate in the management of non- alcoholic fatty liver disease.

4. **Title :Investigating effect of Triphala in patients suffering from Non-alcoholic fatty liver disease (NAFLD): a proof of concept clinical study. Project ID (ObDb/24/1/I); Funding:BVDU- Minor Duration:February 2024 – ongoing; Sanctioned Amount:Rs. 100000/-Investigators:PI: Dr. Poonam Gupte Co-I 1*:Dr. Dadasaheb Maindad; Co-I 2$:Dr. Priscilla Joshi; Collaborating Institution(s): *Associate Professor, Department of Medical Gastroenterology, Bharati Hospital & Research Centre, Bharati Vidyapeeth (Deemed to be) University, Pune $Professor and Head, Department of Radiodiagnosis, Bharati Hospital & Research Centre, Bharati Vidyapeeth (Deemed to be) University, Pune. Project Staff:N/A Ethics Approval:BVDUMC/IEC/80 (20/04/2023) CTRI registration : CTRI/2023/06/054489**

Background: As described in previous project, NAFLD is a global health problem. Our department has carried out extensive work on the formulation Triphala; *Terminalia chebula* (Haritaki), *Phyllanthus emblica* (Amalaki) and *Terminalia bellerica* (Bibhitaki). In an *in vivo* study conducted in our department in a high fat diet induced model, it was seen that Triphala caused a reduction in lipid droplets in the histopathology of liver, thereby indicating a decrease in extent of fatty liver changes. The effect of Triphala with respect to mechanistic involvement of insulin resistance leading to hepatic fat accumulation, responsible for NAFLD was thus proposed for evaluation, in individuals diagnosed with NAFLD.

Objectives:

- To determine the effect of Triphala on fatty liver changes
- To evaluate the effect of Triphala on insulin resistance

Work done: The study is ongoing. Out of 23 approached individuals, 10 were eligible and recruited in the study. So far, 5 individuals have completed the study and 2 individuals are ongoing and expected to complete in this month.

5. **Title : In vivo efficacy studies of novel phytoformulations of selected phytoactives in model of high fat diet induced fatty liver. Project ID (ObDb/24/2/I); Funding: BVDU-Minor Duration:April 2024 – July 2024 Sanctioned Amount:Rs. 100000/-Investigators: PI:Dr. Supriya Bhalerao Co-I*:Dr. Varsha Pokharkar; Collaborating**

Institution(s): *Professor & Head, Department of Pharmaceutics, Poona College of Pharmacy, Bharati Vidyapeeth (Deemed to be) University, Pune. Project Staff:N/A
Animal Ethics Approval:BVDUMC/3016/2022/001/005

Background: Non-alcoholic fatty liver disease (NAFLD) represents a global healthcare burden due to its epidemiological relation to conditions like obesity and type 2 diabetes along with its high prevalence in the developed countries. A number of pharmacological agents are currently being tested for safety and efficacy but these are in the initial pharmacological phases (phase 1 and 2) and it is thus reasonable to assume that the next generation of NAFLD drugs will not be available for clinical use for foreseeable future. Phytoconstituents present in herbals are associated with low oral bioavailability and hence fall short of achieving the desired efficacy. Thus, the use of a drug carrier system using pharmaceutical drug delivery systems is necessary to address these problems. With this objective, we have developed nano formulation of bioactives. The premise of this research work will revolve around evaluating effect of these formulations on fatty infiltration in liver and highlighting their role as novel therapeutic approaches in NAFLD management.

Objectives:

- To assess the effects of high fat diet (HFD) on pathophysiological changes (biochemical, molecular and histological) in the induction of fatty liver.
- To observe effects of phyto- formulations on the progression on NAFLD

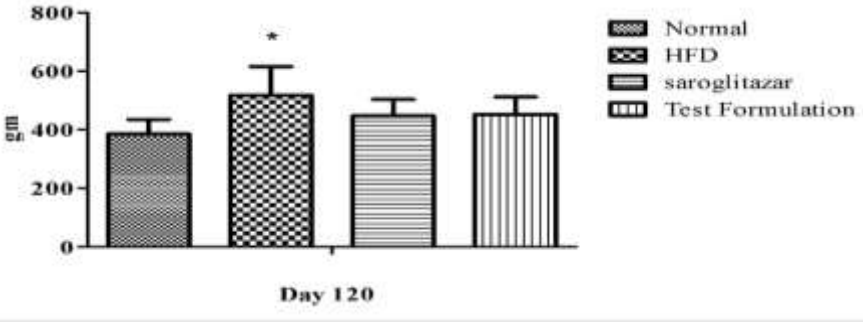
Work done: The study started with the approval from Institutional Animal Ethics Committee (IAEC), (BVDUMC/3016/2022/001/005). The guidelines of the Committee for the Purpose of Control and Supervision of Experimental Animals (CPCSEA), Govt. of India were followed. Wistar Albino rats (aged 5 weeks) weighing between 120-150 g were procured and maintained under appropriate housing conditions (12-hour light/dark cycle conditions at 22 ± 2 ºC temperature) with unrestricted access to food and water. They were randomly divided into respective groups; Normal control (NC- only chow diet), Disease control (DC- only HFD), Positive control (PC- HFD + Saroglitazar) and Test formulation (TF- HFD + as of 6 rats per group after acclimatization. The total duration of the study was 120 days after which the rats were sacrificed. Except NC, HFD was given to all groups till day 120. The PC and TF were started after 60 days of HFD and continued till day 120.

Results: The effect was tested on body weight and biochemical parameters; fasting blood glucose and lipid profile.

Body weight

The body weights of the animals in all groups significantly increased ($p \leq 0.05$) on days 60 and 120. The treatment groups showed a decrease compared to HFD group on day 120. (Figure 1)

Figure 1: Effect of treatment on body weight



Biochemical parameters

An increase was observed in all the parameters in HFD group in comparison to NC group on day 120 which was significant for fasting blood sugar ($p < 0.01$) and triglyceride ($p < 0.05$) levels. Both, the PC group and TF group showed a decrease in all parameters at the end of treatment when compared to HFD group, which was significant for blood sugar ($p < 0.05$) in PC group & for triglycerides ($p < 0.05$) and HDL ($p < 0.01$) in addition to blood sugar ($p < 0.05$) in TF group. (Table 1)

Table 1: Effect of treatment on biochemical parameters

Parameters	NC	HFD	PC	TF
Fasting Blood Sugar	98.2 ± 13.25	149.1 ± 28.55**	110 ± 25.64$^{\#}$	105.6 ± 16.12$^{\#}$
Total cholesterol	54.56 ± 4.79	62.91 ± 6.83	50.63 ± 4.20	51.90 ± 15.29
Triglycerides	100.3 ± 55.5	184.4 ± 36.1*	129.2 ± 21.8	101.0 ± 20.8$^{\#}$
HDL-Cholesterol	23.34 ± 4.60	17.70 ± 4.99	25.15 ± 7.00	33.30 ± 6.52$^{\#\#}$

*$p < 0.05$, **$p < 0.01$ when compared to Normal control (NC) group; # $p < 0.05$, ##$p < 0.01$ when compared to HFD group analysed using Two-way ANOVA, followed by a Dunnett's Multiple Comparison Test

Further, evaluation of effect of the treatment on histopathology of liver and adipose tissue is under process.

6. **Title: Identification of Nadi patterns in individuals with different glycemic profiles using AI based technology and their validation for mass screening of T2DM' with Atreya Innovations Pvt. Ltd. Funding: Atreya Innovations Pvt. Ltd. Project ID**

(ObDb/24/4/E) Duration: January 2024 – ongoing Sanctioned Amount: Rs. 6,03,393/- Investigators: PI:Dr. Supriya Bhalerao Co-I*: Dr. Asavari Joshi Collaborating Department: *Assistant Professor, Centre for Innovation in Nutrition Health Disease.(CINHD), IRSHA, Bharati Vidyapeeth (Deemed to be) University, Pune Project Staff : Dr. Tanuja Sawant Ethics Approval : BVDUMC/ IEC/07 CTRI registration: CTRI/2024/01/062157

Background: As per WHO, there are an estimated 77 million diabetics (Type 2) and nearly 25 million pre-diabetics in India. More than 50% of people are still undiagnosed, which can cause serious health problems if not detected early and managed. The conventional method for diagnosing diabetes is based on blood tests; blood glucose and Glycosylated Haemoglobin (HbA1c) levels, which is invasive, time-consuming and pain-inducing. Atreya Innovations Pvt. Ltd., a Niti Ayog Start-up Grant awardee, has developed a device, Nadi Tarangini, a digital platform for assessment of Nadi (pulse) patterns. Nadi examination is an integral method for prediction and prognosis of diseases in Ayurveda. Apart from Nadi pariksha, other examinations namely Jihwa Pariksha (Tongue Examination), Shabda Pariksha (Voice Examination), Drik Pariksha (Face Examination) which are part of Asthavidha Pariksha or the eight tools of examination recommended by Ayurveda have also been taken into account. In order to implement Nadi Tarangini for the mass screening of Type 2 diabetes using Artificial Intelligence (AI) based technology, the present study has been planned in 2 parts. In part 1, information pertaining to all the above-mentioned parameters was captured in individuals with known glycemic profile and was correlated with HbA1c. In part 2, based on the established pulse patterns, the technology will be used for community screening of diabetes. Further, using Principal Component Analysis, the essential parameters from the above list required to capture for reliable screening of diabetes will be identified and AI based protocol will be standardized.

Objectives:

- To recognize Nadi patterns in individuals with different glycemic profiles using AI.
- To validate the AI recognized patterns for screening of Type 2 diabetes.
- To standardize the protocol for AI based screening of diabetes

Work done: Part I: Post Ethics approval, individuals of either sex, in the age group of 25 - 55 years were approached and explained about the study. After screening them, as per eligibility criteria, eligible individuals underwent Nadi assessment by Nadi Tarangini followed by a random estimation of Glycosylated Haemoglobin.
They were then categorized into following 4 groups:

1. Normal (n= 50) with HbA1c < 5.7 %

2. Pre-diabetics (n= 50) with HbA1c in the range 5.7- 6.4 %
3. Diabetics (n=50) with HbA1c ≥ 6.4 - < 9 %
4. Diabetics (n=50) with HbA1c ≥ 9 %

Further, they were called to the study site for estimation of fasting and post prandial glucose followed by Prakriti (body constitution), dietary & lifestyle evaluation along with face, tongue features photography, voice recording and a 6 minute walk test.

Part II:
Individuals of either sex, in the age group of 25 - 55 years were approached and explained about the study. Eligible individuals underwent Nadi assessment by Nadi Tarangini and other assessments mentioned in Part I followed by random estimation of Glycosylated Haemoglobin.

Results:

The study is ongoing and the number of individuals screened and recruited is as follows-
Screened – 150
Recruited

Part 1

- Normal – 49
- Pre-diabetes – 26
- Diabetes – 22 (HbA1c < 9 %)
- Diabetes – 7 (HbA1c > 9 %)

Part 2 – 246

7. **Title : A comparative efficacy study of Nishamalaki and Metformin in lean and obese females suffering from Polycystic Ovary syndrome (PCOS) along with focus on fatty acid composition Funding:Shree Dhootpapeshwar Ltd. Project ID (ObDb/24/5/E) Duration: May 2024 – ongoing Sanctioned Amount:Rs. 4,35,349.2/- Investigators: PI:Dr. Poonam Gupte PhD student: Vallari Nisargand Co-I 1:Dr. Supriya Bhalerao (Guide) Co- I 2*: Dr. Asavari Joshi (Co-guide) Co-I 3$:Dr. Girija Wagh Co-I 4#:Dr. Vijaya Pandit. Collaborating Department: *Professor & Head, Department of Gynaecology & Obstetrics, Bharati Vidyapeeth Medical College, Bharati Vidyapeeth (Deemed to be) University, Pune $ Professor, Department of Pharmacology, Bharati Vidyapeeth Medical College, Bharati Vidyapeeth (Deemed to be) University, Pune. #Assistant Professor, Centre for Innovation in Nutrition Health Disease.(CINHD), IRSHA, Bharati Vidyapeeth (Deemed to be) University, Pune. Ethics Approval : BVDUMC/ IEC/07 CTRI registration : CTRI/2024/01/062157**

Background: Polycystic Ovary Syndrome (PCOS), is the most common and complex endocrine disease affecting 5–10 % of women of reproductive age. It generally manifests with oligo or anovulatory cycles, hirsuitism and polycystic ovaries, together with a considerable prevalence of insulin resistance. The diagnosis of PCOS must be based on the presence of at least two of the following three criteria: chronic anovulation, hyperandrogenism (clinical or biological), and polycystic ovaries. insulin resistance is considered to play a key-role in its pathogenesis. Also, dyslipidemia is a feature of polycystic ovary syndrome (PCOS) that may augment metabolic disturbances. Different treatment modalities have been proposed for PCOS, of which Metformin, an insulin sensitizing agent has shown beneficial effects for the same. Shree Dhootpapeshwar Limited have marketed a formulation, Nishamalaki, (NA) indicated to improve insulin sensitivity and promote general well-being. The formulation is a combination of Haridra (Curcuma longa) and Amalaki (Phyllanthus emblica), recommended in the classical texts of Ayurveda and considered as the first line of treatment for diabetes. Insulin resistance is the common etiological factor for both diabetes and PCOS. A previous reported study on Nishamlaki yielded good results in the amelioration of glucose, insulin levels and inflammation. It was thereby thought interesting to substantiate the efficacy of Nishamlaki, formulated by traditional method in lean and obese PCOS females compared to Metformin focusing on fatty acid profiles.

Objectives:

To assess the effect of Nishamalaki compared to Metformin on insulin resistance, Inflammation and oxidative stress markers in Lean and Obese patients with PCOS

To compare Fatty Acid profile in Lean and Obese PCOS patients

To correlate fatty acid level outcomes with Insulin resistance, Inflammation and oxidative stress markers in Lean and Obese PCOS patients

To compare response to treatment in Lean and Obese PCOS patients

Work done: The study was initiated after Ethics approval. So far, 75 females have been approached from the community and out- patient department of Gynaecology, in the age group of 18- 45 years. Ten females, who voluntarily showed interest to participate were screened for Ultrasonography (USG) of Abdomen and pelvis region. Following confirmation of polycystic ovarian morphology on USG, they underwent blood tests for Thyroid stimulating hormone and Glycosylated haemoglobin. Females with normative values were recruited on the 2nd or 3rd day of menstrual cycle that was either natural or medication induced. They were randomly assigned to either Nishamlaki or Metformin groups in the ratio 2:1. Five females have been recruited of which 1 has completed the study and 4 are ongoing. The total sample size to be completed is 60; 40 in Nishamlaki group and 20 in Metformin group.

8. **Title: Prevalence of Single Nucleotide Polymorphisms in lipid metabolizing genes in patients with Type 2 Diabetes Mellitus. Funding: Central Research Publication Unit (CRPU), BVDU. Project ID (ObDb/24/5/E) Duration:May 2022- ongoing; Sanctioned Amount:Rs. 3,30000/-Investigators: PI:Anu Moses (PhD student) Co-I 1:Dr. Supriya Bhalerao (Guide) Co-I 2*:Dr. Rakhee Dangi (Co-guide) Collaborating Department : *Associate Professor, Department of Molecular Biology, Rajiv Gandhi Institute of Information Technology and Biotechnology, Bharati Vidyapeeth (Deemed to be) University, Pune Ethics Approval : BVDUMC/IEC/57**

Background: The definition of IR, a T2DM component, has historically been glucocentric, with glucotoxicity playing a leading role. However, studies have shown that "lipotoxicity" contributes considerably to IR. Observational studies have linked greater levels of circulating lipids to an increased risk of IR and T2DM. Elevated free fatty acid (FFA) levels cause ectopic fat deposition in key organs and have been shown to disrupt insulin signaling. But, the mechanisms by which FFA impairs insulin functioning is not well understood. The capacity of adipose tissue to store extra calories determines how well the body can adjust to long-term alterations after high calorie consumption. In people with a genetic propensity for T2DM, abnormal abdominal adipose cell hypertrophy and dysregulated adipose tissue were four times more prevalent. Genetic predisposition makes an individual susceptible to the environment that even small increases in body fat promote reduced insulin sensitivity phenotype with an increased risk to develop T2DM. However, relatively few studies have demonstrated a relationship between the genes involved in lipid metabolism and IR.SNP analysis in lipid metabolizing genes can give insight to its relationship with T2DM pathogenesis.

Objectives:

- To study the prevalence of selected SNPs in patients with T2DM
- To explore the difference in prevalence of the SNPs with respect to sex and Body Mass Index

Work done: Post Ethics approval, a systematic assessment of several pathway, gene, and SNP databases was conducted to identify SNPs of lipid metabolism linked with T2DM in the Asian-Indian population. The identified SNPs (CD36 rs1761667,FADS2 rs174575, APOA5 rs662799) will be further screened for each participant, and additionally blood markers will be evaluated for control group. Hardy-Weinberg Equilibrium will be used to calculate the allele frequency in study population. There are 2 study groups; normal control group vs diabetic individual group.

A total of 176 participants have been recruited so far of which 87 are normal and 89 are diabetic.

DNA isolation for all the recruited participants has been completed till date. CD 36 gene polymorphism (rs1761667) was analyzed for 69 patients of which 32 were normal participants and 37 were of diabetics. rs1761667 polymorphisms were found in 24 diabetic patients which is higher than that found in 10 normal participants.

9. **Title : A three-arm, randomized, controlled clinical study to evaluate the effect of Tablet Pulcerid in the management of non-erosive reflux disease (NERD) with AVN Ayurveda Formulations Pvt. Ltd. Project ID (ObDb/24/6/E) Funding:AVN Ayurveda Formulations Pvt. Ltd. Duration:Yet to start Sanctioned Amount: Rs. 8,34,594/- Investigators: PI: Dr. Supriya Bhalerao Co-I 1*:Dr. Dadasaheb Maindad Co-I 2[$]: Dr. Prachee Makashir Co-I 3[#]:Dr. Sonali Palkar Collaborating Institution(s): *Associate Professor, Department of Medical Gastroenterology, Bharati Hospital & Research Centre, Bharati Vidyapeeth (Deemed to be) University, Pune [$]Professor, Department of Medicine, Bharati Hospital & Research Centre, Bharati Vidyapeeth (Deemed to be) University, Pune [#] Associate Professor, Department of Community Medicine, Bharati Hospital & Research Centre, Bharati Vidyapeeth (Deemed to be) University, Pune**

Background: Gastroesophageal reflux disease (GERD), a very common benign disease of the upper gastrointestinal tract whose prevalence in India ranges from 7.6% to 30%. Non-erosive reflux disease (NERD) also called 'endoscopy negative' reflux disease is a heterogeneous group of disorders, presenting with symptoms of heartburn, regurgitation or both, in the absence of visible esophageal injury upon endoscopy. The burden of illness on health-related quality of life also has an impact on productivity, both at and outside work. Among the therapeutic options available, Proton-pump inhibitors (PPIs) have been proved as a safe and effective way to treat patients with NERD and are recommended as the main acid suppressive drugs. However concerns have been raised about PPI overuse and the associated increased risk of harm, not only in terms of increased costs but also the potential risk of physical dependence and long-term side effects of PPIs. Pulcerid tablets, a known polyherbal proprietary formulation produced and marketed by AVN Ayuveda.indicated for acid peptic disorders is a combination of 26 medications of herbal and mineral origin consisting of medicinal herbs like Amalaki (Phyllanthus emblica), Yashtimadhu (Glycyrrhiza glabra), Amruta (Tinospora cordifolia), Dhanyaka (Coriandrum sativum) etc. Multiple studies on each of the herbs have been reported emphasizing their therapeutic potential in gastric disorders. This study is thereby planned to generate evidence regarding efficacy and safety of Pulcerid tablets in non- erosive reflux disease compared to PPIs.

Objectives:

- To assess the effect of Pulcerid tablets on clinical symptoms in patients of non-erosive gastro-oesophageal reflux disease

- To assess the effect of Pulcerid tablets on quality of life in patients of non- erosive gastro- oesophageal reflux disease
- To determine the safety and tolerability of Tablet Pulcerid in patients of non-erosive gastro- oesophageal reflux disease

The funds have been received. The project is approved by Scientific Review Committee of Bharati Hospital & Research Centre and is due for submission to the Ethics Committee for approval

10. **Title :Evaluation of Phonophoresis Therapy with Myostaal Gel in Participants suffering from Acute Musculoskeletal Conditions: A Randomised, Controlled Clinical Study. Project ID (ObDb/24/7/E) Funding:Solumiks Herbaceuticals Pvt. Ltd. Duration:August 2022- May 2023 Sanctioned Amount: Rs. 4,80,520/-. Investigators: PI-:Dr. Poonam Gupte Co-Investigator 1:Dr. Supriya Bhalerao Co-Investigator 2*:Dr. G.R.Joshi Co-Investigator 3$: Dr. Neeraj Athavale Collaborating Institution(s): *Department of Orthopaedics, Bharati Vidyapeeth Medical College, Bharati Vidyapeeth Deemed to be University, Katraj, Pune- 411043 $School of Physiotherapy, Bharati Vidyapeeth Deemed to be University, Katraj, Pune- 411043 Project Staff: Dr. Revati Bhat Ethics Approval: BVDUMC/IEC/205 (23/08/2022) CTRI registration: CTRI/2022/09/045330. The project was completed in May 2023 and the final instalment was received in September, 2023.**

Name of the Programme: Herbal Medicine

1. **Title: Development of a novel synbiotic using Dioscorea as a prebiotic against Ulcerative Colitis. Project ID (HM/21/1/P) Funding: UGC Duration: 01-11-2021 to 13-08-2024. Sanctioned Amount: Rs. 5, 20, 800 Investigators: NA PICo PI- NA Ph.D. Students: Apurva Jadhav Human Ethical Approval: NA**

Background: Synbiotics have been found to reduce levels of inflammation, improve digestion, and improve the balance of bacteria in the gut, all of which can help reduce the symptoms of ulcerative colitis. Prebiotics are naturally occurring complex carbohydrates found in plants and the *Dioscorea* spp. Plants of Maharashtra will be an excellent source of prebiotics. The secondary screening will be conducted for anti-inflammatory properties, and consent will be obtained from the Maharashtra State Biodiversity Board. The plant parts will be assessed for their prebiotic potentials and combined with probiotics to create synbiotic formulations. The best and most effective formulations will be evaluated for their anti-inflammatory potential in vivo.

Work done: The present investigation is aimed to purify and assess the prebiotic potential of *Dioscorea* collected from Maharashtra; hence different species of *Dioscorea* plant have been collected, extraction of prebiotics is done, and further optimization of the dosage for probiotics, prebiotics and synbiotics in an in-vivo *Drosophila melanogaster* model is going on.

Results: Among different species of *Dioscorea* collected from Maharashtra, we have prioritized selected species based on their prebiotic potential and in vivo studies in the *Drosophila* model.

Conclusion: The *Dioscorea* plant has good prebiotic potential, and now work is underway for its synbiotic potential.

Name of the Programme: Centre for Innovation in Nutrition Health Disease (CINHD)

1. **Title: ICAR -AICRP- Linseed Value Addition Centre; Project ID: INHD/15 (15-18)/1/E Funding: ICAR, New Delhi Duration: April 2015 onwards Scientist in-charge: Dr. Anand A. Zanwar Amount received: Total 171.52 Lakh (2015-24), 29.98 Lakh (2023-24)**

Background: Broad objective is linseed value addition. The following technical program for 2023-24 was planned and approved during Annual Linseed Group meeting of Linseed organized by Indira Gandhi Agricultural University, Raipur, Chhattisgarh during September 5-6, 2023.

Objectives:

A. Blending of linseed oil with edible oil
B. Development of linseed derived omega-3 health supplements
C. Development of value added cake from linseed
D. Development of value added bread from linseed
E. Nutritional evaluation of released linseed varieties in India

A. Blending of linseed oil with edible oil

This technical program is divided into two parts. The 1st one involves, development of linseed oil based edible oil blends, its characterization and long-term storage stability study with added antioxidants. This part is completed, and recommendations are drawn already. The 2nd one involves studying the thermal stability of blended edible oil with linseed oil, which was started in 2019-20. In order to assess the stability of omega-3 fatty acid during thermal treatment, various combinations of antioxidants such as TBHQ+Tri E, AP+TBHQ, AP+Tri E, Rosemary extract, Green Tea extract, ginger and black pepper etc. were tried and its effect on primary and secondary oxidation parameters such as such as peroxide value, p-anisidine value, totox value, free fatty acid content, smoke point etc. were studied. Further effect on fatty acid profile, total polar molecules, conjugated dienes, conjugated trienes, and trans fats during thermal treatment continuous for 8 hr was also studied. The stability of omega-3 fatty acid in fried products under domestic frying conditions were also studied using 5 cycles per day for 6 days (keeping gap of 5 minutes in each cycle constituting total 30 cycles for each group). This year 2023-24, these three blends were subjected for Rancimat analysis at 160 °C and final characterization of blends i.e. oil quality analysis using physicochemical properties and fatty acid analysis.

The oil stability index (OSI) method, also commonly known as the Rancimat method, allows oxidative stability to be determined automatically under standardized conditions (AOCS, 1992). In this method, because of sudden rise of volatile acids due accelerated heating occurs at high temperature under constant aeration. Such molecules are trapped in water and monitored by electro-conductivity. It is a standard parameter of quality control

in the production of oils and fats in the food industry or for food inspection in modern processing plants.

In the present study, OSI was carried out for selected blends with/without added antioxidants. LO had the lowest induction time as expected i.e. 0.15 hr only. In case of the PO, induction time was 0.96 hr and addition of LO in PO reduced same to 0.42 hr, combination antioxidant AP+TBHQ was found to be most efficient than that of BP as it increased induction time to 1.23 hr which higher than that of plain PO and BP recorded much lower induction time i.e. 0.27 hr only. In case of the RBO, induction time was 0.96 hr and addition of LO in RBO reduced the same to 0.52 hr and among the two selected antioxidants, combination antioxidant AP+TriE was more effective than that of BP. In the case of CO, induction time was 3.62 hr and addition of LO in CO very significantly reduced induction time to 0.63 hr and combination antioxidant (AP+TriE) showed comparative improvement in induction time i.e. 1.34 hr, however this value is much lower than control value indicating CO+LO blend is not oxidatively stable with/without antioxidant in thermal studies.

Finally, these oil blends were subjected to characterization. Both PO and RBO blends were within the acceptable limits w.r.t. oil quality parameters i.e. peroxide value (<2 mEq/kg), free fatty acid (<0.1), smoke point (above the domestic temperature i.e. 180°C under continuous heating/frying). Further the fatty acid profile recorded O6 to O3 ration less than 2:1 in both the blends (Table 1).

Table 1: Final characterization of linseed oil-based blends

	Units	**PO+LO**	**RBO+LO**
Physicochemical properties			
Peroxide value	mEq/kg	1.7±0.14	2.0±0.14
Free fatty acid	%	0.05±0.0	0.06±0.0
Smoke point	(°C)	225	255
Cloud point	(°C)	15°C	1°C
Iodine Value	-	80.23	113.19
Saponification Value	-	195.03	183.1
Fatty acid			
SFA	%	38.22±0.33	20.95±0.23
MUFA	%	40.81±0.33	34.69±0.53
PUFA	%	20.97±0.01	44.37±0.30
O-3	%	9.77±0.04	14.76±0.01
O-6	%	11.20±0.04	29.61±0.32
O6/O3	%	1.15±0.01	2.01±0.02

Conclusion: Based on the results obtained so far, in case palm olein based blend the combination antioxidant i.e. AP+TBHQ and in the case of rice bran oil blend the

combination of antioxidant i.e. AP+TriE is recommended for thermal stability study as these added antioxidants showed protection to omega-3 fatty acid at domestic heating temperature under continuous frying conditions/continuous heating trials as well.

B. Development of linseed derived omega-3 health supplements

In this technical program, for incorporation of omega-3 fatty acid in plain and flavored milk, initially 3 types of water-in-oil type of emulsion i.e. linseed oil emulsion, linseed oil + vitamin emulsion and linseed oil + protein emulsion etc. were prepared. These emulsions were characterized (proximate analysis, nutritional analysis and particle size assessment) and studied for stability assessment (oxidative stability study and fatty acid profile for 12 months). This work was done during 2020-21 to 2022-23. Now the performance of these emulsions is being assessed in plain (domestic heating trial) and flavored milk (storage stability study upon autoclaving) is currently assessed this year.

Studies on incorporation of omega-3 emulsion in flavored milk

Each emulsion, i.e. linseed oil emulsion, linseed oil + vitamin emulsion and linseed oil + protein emulsion etc. were added to flavored milk which was then autoclaved, bottled and fully packed flavored milk bottles were subjected for proximate analysis, and same was also subjected for stability study to understand the stability of omega-3 fatty acid for 4 months. Proximate analysis of fortified flavored milk before and after autoclaving recorded comparable and non-significant alterations across the groups. Proximate analysis showed total solids ranging between 18.81 to 19.49%, ash content 0.55 to 0.62%, fat content 2.64 to 3.65%, carbohydrate 12.12 to 13.72% and protein 2.44 to 2.69%.

Stability study of fortified flavored milk

The stability study of fortified flavored milk was carried out at 4-8 °C for the period of 4 months. In this study, initially the effect of autoclaving on fatty acid was studied and thereafter fatty acid analysis was carried out upto 4 months. Similar experiments were carried out earlier with altered dose levels and the milk used for these trials varied. This was again repeated this year for validation and confirmation purposes. After autoclaving there were marginal alterations across all the groups was noted including plain flavored milk. Comparative analysis of autoclaved milk (initial) and at the end of 4 months, the overall fatty acid profile including LA, ALA content and omega-6 to 3 ratio showed comparable alterations in experimental groups as that of control group. This indicates the stability of omega-3 fatty acid at the end of 4 months in all the 3 forms of the emulsions based on the results obtained this year.

Similarly in the case of thermal stability study which was done earlier with different dose levels and this year in 2023-24 again repeated for validation and confirmation purpose, each emulsion i.e. oil-in water type linseed oil emulsion, linseed oil + vitamin emulsion and linseed oil + protein emulsion was added to plain milk. The plain milk (without added emulsion) and fortified milk (added emulsion) were evaluated from proximate analysis. Further in order to understand the stability of omega-3 fatty acid upon heating for domestic use, a thermal stability study using 3 heating cycles was carried out. In this study, plain

milk/fortified milk was heated and cooled to room temperature, 3 times. The milk samples were collected initially (no heating) and at the end of each cycle and subjected for fatty acid analysis using gas chromatography.

The addition of emulsion in plain milk increased the total solid content as compared to plain milk. Ash content remained unaltered in all the groups. A slight increase in fat and carbohydrate content was observed as compared to plain milk in all experimental groups and protein content non-significantly reduced in all experimental groups. In the thermal stability of omega-3 fatty acid during heating was studied, there were not many alterations in control milk and subsequent heated milk. In the case of plain emulsion and Vitamin emulsion group, marginal alterations were noted in SFA, MUFA, O-6 content and slight reduction in ALA content in 2^{nd} and 3^{rd} heating was noted. In the case of protein emulsion group, MUFA and O-3 content was slightly reduced after 1^{st} heating only remained constant in 2^{nd} heating and restored to initial value in 3^{rd} heating. Further SFA content increased after the 1^{st} heating and restored to initial value in the 2^{nd} and 3^{rd} heating.

Conclusions (2020-21 to 2023-24): In this study, 3 emulsified formulations were developed, characterized and assessed for stability assessment. Further studies on the addition of these formulations in flavored milk and plain milk and thermal stability study in plain milk and storage stability of flavored milk was carried out.

Addition of omega-3 emulsions improved nutritional characteristics of milk, these 3 formulations were found to be stable for 9 months at 4-6°C. Addition of plain emulsion (linseed oil) and vitamin emulsion (linseed oil+ vitamin premix) can be considered for fortification of milk-based beverages as comparable alterations were noted across the trials despite milk from different dairies was used every year. Addition of these two emulsions improved corresponding omega-3 content. However, linseed oil + protein emulsion showed variation across the 3 trials and there was not significant increase in protein content in protein emulsion group hence can't be considered for its application in dairy/milk beverages.

C. Development of value added cake from linseed

Earlier value added cake was attempted using linseed based premixes/oil/emulsion for incorporation of omega-3 fatty acid in cake. Based on the experimental results, multigrain premix and linseed premix based were shortlisted and this year optimization trial with commercial bakery unit using linseed premix for developing value added cake was carried out and subjected for proximate analysis, fatty acid profile, universal texture analysis, colour analysis and stability assessment for 7 days.

In proximate analysis as compared to control group, experimental groups showed alterations in fat, carbohydrate and ash content. There were non-significant alterations in protein, carbohydrate and fat between control and 5%, 10% premix groups. However dietary fibre content showed reduction as compared to control group. In the case of fatty acid profile SFA content showed reduction in 5%, 10% premix groups vs control group.

Omega-3 fatty acid content showed a significant increase and O6/O3 ratio was also significantly reduced as per the addition of premix. More important the trans-fat content was within the acceptable limit in both the premix groups (acceptable limit <1%) and comparable with control group. This clearly indicates the stability of omega-3 fatty acid during the backing trial. In case of colour analysis both bottom and top part of cup-cake was considered for analysis as top part in cup cake is darker than that of bottom part and there were non-significant alterations between control and premix groups. In the stability study of cup-cake when stored at ambient conditions, there were non-significant changes between the respective groups at the end of 7 days compared to the initial values. This study will be continued for next year to optimize the final prototype.

D. Development of value added bread from linseed

Earlier we have developed omega-3 fortified bread (refined wheat/maida and wheat based) using fully automatic bread maker and for appropriate incorporation of omega-3 fatty and dietary fibre in bread using linseed-based premix which can be used for preparation of omega-3 fortified bread. This year we prepared omega-3 bread (wheat and refined wheat based) at the commercial bakery unit for optimization of the protocol for value added bread development.

Results: In the present study, linseed-based premix (5% and 10%) was used for commercial trial of preparation of bread at bakery unit. Both maida (refined wheat) and wheat-based bread were prepared and subjected for proximate analysis, fatty acid profile, colour analysis and stability assessment for 7 days.

The proximate analysis showed comparable data across the groups and there was gradual increase in the fat content and dietary fibre content as per the % of premix added in the bread and reduction in carbohydrate content was observed due to increased dietary fibre content in 5% and 10% premix group. In the case of fatty acid profile, reduction in SFA content and increase in ALA and PUFA content in premix group as compared to control group and was recorded. The O6/O3 ratio was significantly reduced in both the premix groups. Finally trans-fat analysis in both premix groups was within acceptable range indicating stability of omega-3 fatty acid during baking and comparable to that of control group was recorded.

In the case of colour analysis, as expected due to brown colour of linseed premix as per the additions made in wheat bread, there was alteration in colour parameters (L*, a*, b* and DE*ab). Table 2.10 represents the stability of omega-3 fatty acid at the end of 7 days. In case of storage stability study, there was non-significant alterations in the overall fatty acid profile across the groups including O-3 and O6/O3 ratio as compared to initial values, indicating stability of the omega-3 fatty acid over the tested period. Slight variation in SFA content was noted in 5% premix group and control group.

Conclusion: In this study using linseed-based flour premix was used for incorporation of omega-3 fatty acid in bread. Earlier we used blended oil approaches for incorporation of omega-3 fatty acid in bread which was not found suitable. This program was extended for

developing the wheat-based bread and optimization of bakery prototype as well. Now both wheat and refined wheat-based bread's commercial bakery trial for optimization of protocol and its complete characterization was carried out. Further stability study of these breads was also found to be equivalent to control bread and linseed-based flour premix was found to be stable for the period of 6 months when kept un-opened for the said period. Refined wheat bread and wheat bread are now ready for commercialization.

E. Nutritional evaluation of released linseed varieties in India

This program was initiated during 2020-21 and so far, we analyzed 16 linseed varieties namely, Divya, Garima, TL-99, Shekhar, Padmini and JLS-95, Ruchi (LCK-5021), Indu (LCK1108), Rajan (LCK-1009), Mau Azad Alsi (LMS149-4), Azad Alsi-1 (LMS9-2K), Gaurav, Shikha, Subhra, Priyam and Sweta etc. and this year (2023-24) 5 linseed varieties namely JLS79, JLS67, JLS9, JLS27 and JLS73 were considered for overall nutritional evaluation purpose. Among the tested varieties during 2023-24, the protein content was ranging between 17.54 (JLS9) - 21.75% (JLS79). The fat content varied between 38.98 % (JLS79) – 44.3% (JLS9). In the case of dietary fiber, there was not much variation in dietary fiber ranging between 24.39% to 26.24%. The lowest dietary fiber content was in JLS27 variety and highest in case of JLS9 linseed varieties. There was not much variation in energy value (more than 550 Kcal/100g) and ash content (more than 3%) between the tested varieties. The important mineral such as calcium, iron, potassium and zinc etc. were analyzed and calcium ranged between 247.41 mg/kg (JLS27) to 434.18 mg/kg (JLS79), iron was ranging between 16.1 mg/kg (JLS27) to 40.42 mg/kg (JLS79), potassium ranged between 68.96 mg/kg (JLS27) to 114.23 mg/kg (JLS79) and zinc ranged between 291.13 mg/kg (JLS73) to 543.06 mg/kg (JLS79). Further fatty acid analysis was also carried out. The saturated fatty acid ranged between 10.53±0.04% (JLS73) to 12.29±0.21% (JLS27), mono-saturated fatty acid levels ranged between 16.28±0.75% (JLS73) to 26.09±0.12% (JLS27), Linoleic acid (omega-6 fatty acid) levels ranged between 12.49±0.30% (JLS9) to 14.88±0.04% (JLS79) and α-linolenic acid (omega-3 fatty acid) was ranging between 48.87±0.53 (JLS27) to 60.55±0.74 % (JLS73). The α-linolenic acid content was 60.55% in JLS73 linseed variety, this is an important and to be explored for its potential application for value addition.

The functional properties of linseed powder were also tested in these linseed varieties. There is a similar trend of variation in these properties across the tested varieties due to various reasons which includes relative ratio of different constituents like protein, carbohydrates, fat and seed properties of these varieties. There was not much variation in bulk density which was varying between 0.69±0.01 g/ml (JLS9) to 0.76±0.04 g/ml (JLS27). In the case of oil absorption capacity and water absorption capacity, there was much variation across the tested varieties. The oil absorption capacity was ranging between 1.79±0.07 g/g (JLS9) to 2.31±0.03g/g (JLS73) and the water absorption capacity was ranging between 2.74±0.03g/g (JLS79) to 4.16±0.09 g/g (JLS9). There was significant variation in case of emulsion activity and emulsion stability. Emulsion activity was ranging

between 4.50±0.70% (JLS9) to 27.50±0.71 (JLS73) and emulsion stability was ranging between 0.70±0.14% (JLS9) to 4.50±0.41 (JLS67). Further least gelation concentration 10.00±0.00 (JLS9 and JLS73) to 20.00±0.00 (JLS27) and water solubility index varied between 12.20±0.28 (JLS9) to 19.90±0.14 (JLS27).

Conclusion: So far, we have tested 21 released varieties from the last four years. This program will be continued to evaluate the remaining released linseed varieties. The functional assessment showed wide variation and fatty acid profile especially α-linolenic acid content was significantly higher in this year's tested variety. These varieties need to evaluate based on the particular properties and the nutrient profile; these varieties can be explored/recommended for developing the value added food formulations.

F. Assessing performance of oil extracted from TL-99 for edible purpose (low ALA linseed variety)

BARC, Mumbai released a low ALA variety "TL-99". This is a low ALA content linseed variety which can be explored effectively for developing edible linseed oil. This can be very useful for promoting and commercializing the linseed edible oil and increasing the linseed demand from edible oil industries. So, this new program was designed to generate data on physicochemical characterization of oil extracted from TL-99 variety and its storage stability study (keeping quality study with or without added antioxidants). Accordingly, AICRP BVDU, Pune requested for nucleus TL-99 linseeds to AICRP centres. Earlier, seeds received from AICRP Sagar, AICRP Nagpur and BARC Mumbai centre were analyzed, and ALA content ranging between 8.92 to 14.61% and this year TL-99 linseed was available only with Raipur centre. So, we procured these seeds from AICRP Raipur Centre and evaluated them for fatty acid profie. The ALA content was 36.27±0.31% which is much higher and needs fresh seeds with ALA content approximately 5% to initiate this program.

2. Title: Polyunsaturated fatty acid enriched nano-formulation for diabetes: In vivo efficacy and bioavailability studies Project ID: CINHD/22/2/E Funding: Chellaram Diabetic Research Centre Sanctioned amount: 27.38 Lakh PI: Dr. Anand Zanwar Ph.D. Student: Ms. Prajakta Sadashiv Gaikwad Duration: 08-06-2022 to 07-06-2025

Background: In view of the higher omega 6: omega 3 ratio has created a necessity to include omega 3 content in the therapeutics for better human health. In the present study, the work done as reported in the previously, included the objective of development of the formulations using both flax oil and krill oil. Three formulations from each group were developed with varying percentage of added oil content in the respective batches. flax oil (FO-A – 20%, FO-B – 30% and FO-C-25%) of oil content and krill oil (KO-A – 2.5%, KO-B- 5% and KO-C 10%) of krill oil content. Further, the developed formulations were assessed for its initial parameters like particle size analysis and fatty acid profile. The results depict particle size of all the formulations that fell in the nano-range of 20-200 nm. Also, the total percentage fatty acid content was assessed using gas chromatographic

analysis, and the total percentage of ALA content obtained was in accordance with the added flax oil content and, hence concluding the objective.

Work done: In the given tenure the following work has been done.

Stability study of the developed formulations

- The stability study started after the initial development and the characterization of the formulation was completed. It was completed and reported in the last tenure.
- Further the formulations were stored at 40°C ± 2°C and 65% RH, 30 °C ± 2 °C and 35% RH ± 5% and 5ºC ± 3ºC as per ICH guideline for the stability study
- The stored batches were then characterized with respect to particle size and % fatty acid at pre-defined timepoints
- At the end of the study, parameters like color, viscosity, oxidative stability study assays were analyzed

Acute oral toxicity study

- The study was conducted according to the Organization for Economic Cooperation and Development (OECD) revised up-and-down procedure for acute toxicity testing (OECD guideline 425). A dose limit of 2000 mg/kg of each formulation was administered in five healthy non-pregnant female adult Wistar rats. Rats were fasted overnight from food, but not water, prior to dosing and weighed before the formulations were administered orally.

The above-mentioned work has been completed and further study related to efficacy using STZ induced anti-diabetic animal model would be carried out in the next tenure

Results: Stability study of the developed formulations

In this tenure stability study was completed according to the ICH guidelines at 40°C ± 2°C and 65% RH ± 5% RH condition along with 30 °C ± 2 °C and 35% RH ± 5% and 5ºC ± 3º C. Further, on regular intervals of time, the formulations were analyzed for all the mentioned parameters.

The particle size analysis showed gradual increase seen during the stability study. After 90 days, all the batches showed an increase in particle size and separation was observed. Further, separation was observed at the end of the study at all the conditions. The color estimation at the end of the study showed change in the color directly implying deterioration in the sample at higher temperature condition. Additionally, the increase in viscosity can be attributed to the increase in kinetic energy of the molecules because of the higher temperature in the stability chamber, which weakens the inter molecular attractions. In case of fatty acid analysis, decline in the saturated fatty acid due to the presence of caprylic acid which in turn increased the % polyunsaturated fatty acid content was observed. But overall, the omega 6: omega 3 ratio was below 1 indicating the incorporation of omega 3 in the developed formulation.

For both the formulations, the results obtained in the DPPH assay have shown higher % inhibition, which could be contributed by the antioxidant along with the oil content added in the formulation. Formulations showed better antioxidant activity in spite of the limited amount of oil % due to the presence of alpha- lipoic acid added. In case of transmission electron microscopy, the results obtained showed mono dispersed populations of droplets with the diameter as close to the observed droplet size results obtained. The images showed a stable nature of the formulation. These results were obtained during the stability study period and also as a part of characterization

Acute oral toxicity study

Lethal dose (LD_{50}) is the dose that kills 50% of test animals and is used to assess the acute toxicity. After, the rats were orally supplemented with a single dose of the formulations of flax oil and krill oil. There was no signs of toxicity or death of rats observed during the 14-day acute toxicity experimental period. After 14 days of the formulation administration, approximately 5 ml of blood was withdrawn and the hematology analysis of the blood withdrawn was performed immediately. CBC was performed using automated veterinary hematology counter to evaluate the following parameters: red blood cell (RBC) count, hemoglobin concentration (HGB), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red blood cell dimension width-standard deviation (RDW) number of white blood cells (WBC), number of platelets (PLT), number of Lymphocytes, number of Monocytes, number of Granulocytes, mean platelet volume (MPV), and platelet dimensions width (PDW). The results showed a very tiny gain in weight in comparison to rats in the control group, but the difference in weight between groups is not significant ($P > 0.05$) when compared to their control group. The automated platelet count showed a significant difference in the count in comparison to the control group. Not much difference was seen in the evaluated parameters, between the control group, plain oil group and the developed batches attributing to the absence of the toxicity of the formulations.

Conclusion: In this tenure the developed batches underwent the stability study at the 40°C ± 2°C and 65% RH, 30 °C ± 2 °C and 35% RH ± 5% and 5ºC ± 3ºC as per ICH guideline for the stability study. At the end of the study based on the results we could identify refrigeration as a well-suited condition for the storage of the developed batches. Also, the results obtained in the acute oral toxicity have concluded the absence of any kind of toxicity included in the formulations.

3. **Title: Evaluating effects of linseed oil blends on omega-6 to omega-3 ratio of various tissues in an animal model Project ID: CINHD/21/1/I Funding: BVDU's seed research grant Duration: 2021-2022 Sanctioned Amount: 1,00,000/- Principal investigator: Ms. Asavari Joshi Co-investigator: Dr. Anand A. Zanwar**

Background: Flaxseed oil blends with Palm olein or Coconut oil (P20 or C20) were supplemented to evaluate their safety and efficacy to improve tissue fatty acid profile. It was observed that

throughout the study period, supplementation animal groups had lower feed intake compared to control group though body weights were comparable among all the groups. Additionally, there was no adverse effect detected on hematological and biochemical parameters studied. Most importantly, except for the brain, the fatty acid composition of the organs studied reflected improved omega-3 fatty acid content and lowered omega-3 to omega-6 ratio.

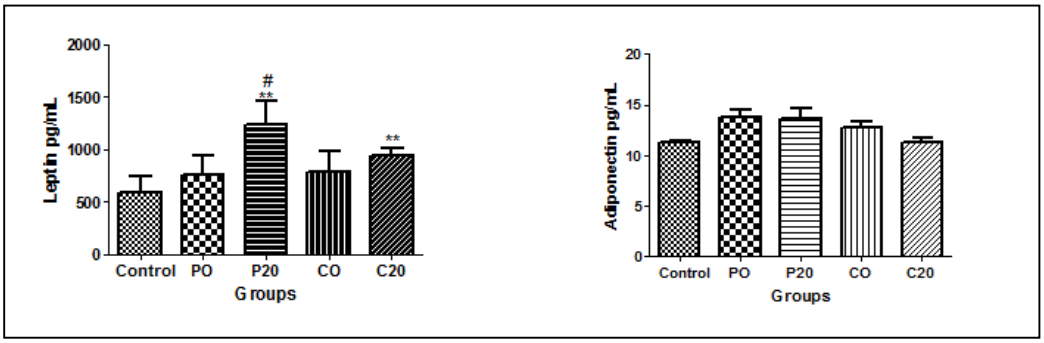
Work done:

1. Evaluation of adipokines- Leptin and Adiponectin
2. Evaluation of inflammatory markers- TNFα and IL-10
3. Histopathological evaluation of liver, kidney, heart and brain

Results: Evaluation of adipokines- Leptin and Adiponectin

Adipokines; leptin and adiponectin were estimated from the serum at the end of three month supplementation using commercially available kits following manufacturer's instructions. Figure 1 represents the effect of blend supplementation on these adipokines.

Figure 1 Determination of adipokines after blend treatments



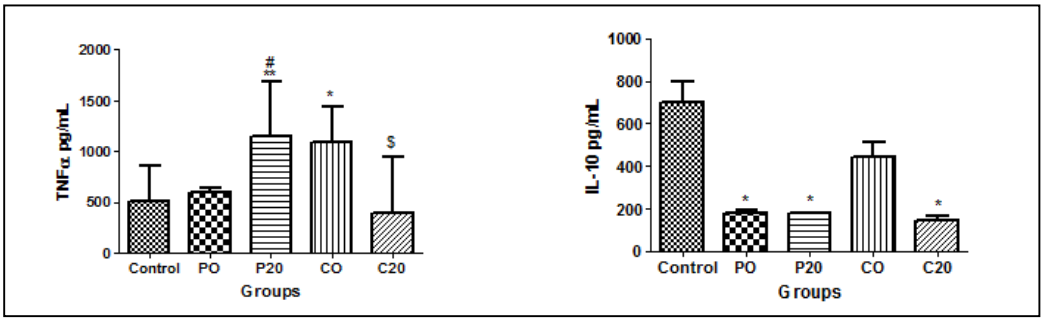
Animals were treated with oil or blend as per the group for the study period (i.e. 90 days). At the end of the study, blood was collected and serum was separated. Leptin (a), Adiponectin (b), TNF-α (c) and IL-10 (d) were estimated in the serum by ELISA. Data is represented as Mean ± SD from three animals. One way ANOVA and Tukey's multiple comparison test was applied to determine statistically significant differences. *; $p < 0.05$ vs Control, **; $p < 0.01$ vs Control, #; $p < 0.05$ vs PO, $; $p < 0.01$ vs CO. PO: Palm olein treated group, P20: Palm olein + 20 % flaxseed oil treated group, CO: Coconut oil treated group, C20: Coconut oil + 20 % flaxseed oil treated group

From Figure 1, it is clear that while the blend supplementation resulted in higher levels of leptin compared to Control, P20 had significantly higher leptin level than PO (only palm olein supplementation group). The adiponectin levels for all the supplementation groups remained comparable to Control group.

1. Evaluation of inflammatory markers- TNFα and IL-10

Inflammatory markers: TNFα and IL-10 were estimated from the serum at the end of three month supplementation using commercially available kits following manufacturer's instructions. Figure 2 represents the effect of blend supplementation on these markers.

Figure 2 Determination of inflammatory markers after blend treatments



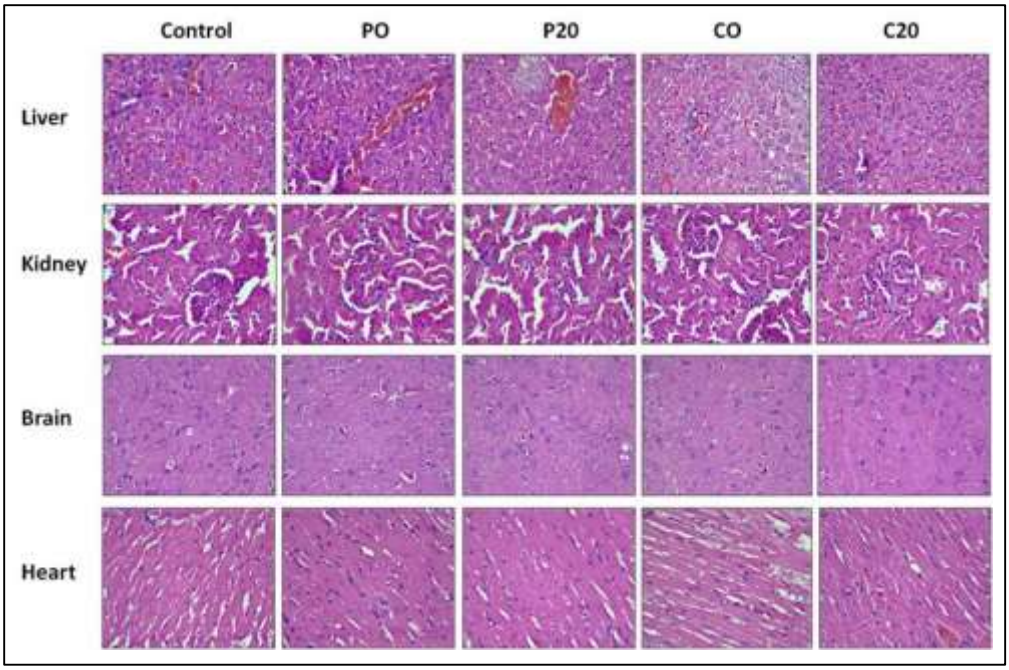
Animals were treated with oil or blend as per the group for the study period (i.e. 90 days). At the end of the study, blood was collected and serum was separated. TNFα and IL-10 were estimated in the serum by ELISA. Data is represented as Mean ± SD from three animals. One way ANOVA and Tukey's multiple comparison test was applied to determine statistically significant differences. *; $p < 0.05$ vs Control, **; $p < 0.01$ vs Control, #; $p < 0.05$ vs PO, $; $p < 0.01$ vs CO. PO: Palm olein treated group, P20: Palm olein + 20 % flaxseed oil treated group, CO: Coconut oil treated group, C20: Coconut oil + 20 % flaxseed oil treated group

From Figure 2, it can be seen that, P20 had significantly higher TNFα level than PO (only palm olein supplementation group) as well as Control group. CO supplementation resulted in significant upregulation of TNFα compared to Control group while C20 had significantly lower level of this inflammatory marker compared to CO group. Interestingly, the anti-inflammatory marker was observed to be lower in all supplementation groups compared to Control group and effect was significant for PO, P20 and C20 supplementation groups.

2. Histopathological evaluation of liver, kidney, heart and brain

10 % formalin fixed tissues (liver, kidneys, brain and heart) from all the groups were processed routinely and embedded in paraffin. The sections of 3-5 µM thickness were cut and stained with hematoxylin-eosin stain. A Histopathology examination of all the organs was carried out by a board certified Toxicopathologist. Representative stained sections of the above-mentioned organs are presented in Figure 3.

Figure 3 Histopathological examination of Liver, Kidney, Brain and Heart by H&E staining



No lesion of clinical significance was detected in any of the tissues studied. Infiltration of inflammatory cells, lipid accumulation, congestion of micro-vessels and fibrosis were considered.

Conclusion: Adipokines are involved in regulation of feed intake, satiety induction additionally they also possess pro or anti-inflammatory properties. Therefore, adipokines were determined. Blend supplemented groups had higher levels probably resulting in lower feed intake as seen earlier. Additionally, leptin induces expression of TNFα and TNFα stimulate adipocytes to secrete leptin as seen in case of P20 supplementation, but further studies are warranted for observed effects for C20 supplementation. Probably as the study is conducted in healty/normal rats without any inflammatory stimulator, anti-inflammatory cytokines; adiponectin and IL-10 remained comparable or lower than control. The histopatological analysis indicates no adverse effect of blend supplementation of studied key organs.

4. **Title: Developing high oleic safflower genotypes through functional genomics Funding: Institutional; Project ID: CINHD/21/2/I PI: Dr. P. B. Ghorpade Technical Assistant: Mr. Yogesh S. Badhe Duration: 2021 onwards**

Background: Thirteen (13) high oleic safflower lines were selected from M 8 generation. These lines will be maintained as nucleus seed material for future development of high oleic safflower variety.

Work done: In Rabi 2023-24 we have selected thirteen (13) out of 15 high oleic safflower sister lines from M 8 generation. These 13 lines were grown in 2023-24 and

multiplied their seeds as nucleus seed. The Oleic acid content of these 13 lines is given in Table 1.

a) NASF-12 (D) was grown in about half acre and total seed harvested is 140 Kg.

Table 1: The Oleic content of 13 safflower lines

Sr. No	Safflower Lines	Oleic acid (%)
1	NASF-6 (A)	79.25
2	NASF-6 (B)	79.56
3	NASF-7	79.05
4	NASF-8	79.46
5	NASF-11	80.35
6	NASF 12 (A)	79.06
7	NASF 12 (B)	79.10
8	NASF 12 (C)	80.09
9	**NASF 12 (D)**	**82.09**
10	NASF 12 (E)	81.45
11	NASF 29-8 (A)	78.76
12	NASF 29-8 (B)	78.35
13	NASF 29-9	78.41

Conclusion: After continuous follow up in the field for last eight years we are happy to report that a genotype of safflower (NASF-12 D) has been developed with about 82.09% oleic acid which has potential for commercial exploitation.

5. **Title: Developing Omega-3 Edible Oil Blends and Evaluating Their Effects and Safety in Pre-clinical Studies. Project ID: CINHD/18/2/I/P Funding: Departmental Duration: Registered in 2018 Sanctioned Amount: NA Guide: Dr. Anand A. Zanwar; Co-Guide: Prof. M. V. Hegde Name of Ph.D. student: Mrs. Asavari Joshi**

Background: During 2022-2023, effect PO and CO blends on 3T3-L1 cells were studied.

Work done: Thesis writing, reviewing and all other official formalities were completed, and thesis was submitted to the Ph.D. section of BVDU, Pune.

6. **Title: Development of premix for fortification of omega-3 fatty acids and protein in cereal based functional food Project ID: CINHD/18/3/P Funding: Institutional Registration date: 29th Dec 2021 Ph.D. Students: Ms. Gauri Ligade Guide: Dr. Anand Zanwar**

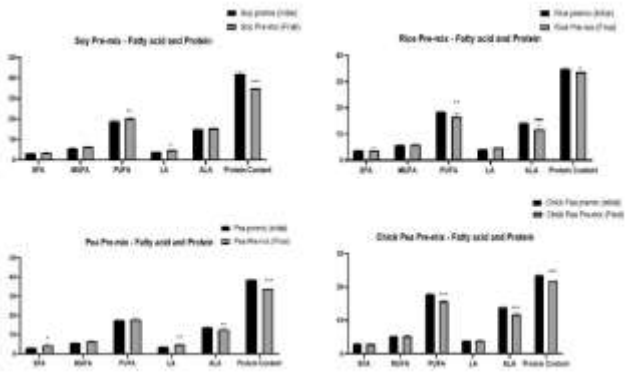
Work done:

Development of Premix for fortification of omega-3 fatty acid and Protein

- *Characterization of flour pre-mix fortified with omega-3 fatty acid and protein*

- Selection of fraction of flaxseed, protein powder and its characterization were carried out in 2022-23. This year formulation of pre-mix and its characterization was carried out with selected flaxseed fraction i.e. dehulled flaxseed powder.
- In the Characterization of Premix (dehulled flaxseed powder and protein (80:20)) formulations includes - soy protein powder, rice protein powder, pea protein powder and chick-pea flour were used in combination with dehulled flaxseed powder
- Following parameters are used for characterization under accelerated stability condition (40℃ and 75% RH) as per ICH guideline
    - ✓ Oil content by Soxhlet extractor
    - ✓ Fatty acid estimation by gas chromatography
    - ✓ Functional assessment includes - bulk density, water solubility index and water absorption capacity, oil absorption capacity
    - ✓ Protein content

Result: Soy protein formulation show highest ALA content (53.59)with non-significant reduction at the end of stability and there is significant decrease in protein content in all premix formulation in which is soy protein is highest around 35%



Conclusion: Based on the results the following premix formulation was selected for further consideration: Dehulled flaxseed powder + protein soy protein (80:20)

Name of the Programme: Translational Virology

1.Title: Immunogenicity testing services provided by NIBEC during 2023-2024. (Project ID: CD/19/1/E) Funding: DBT-BIRAC (Under National Biopharma Mission) Duration: March 2019 – March 2024 Sanctioned Amount: Rs. 16 crore Investigators: PI - Dr A C Mishra; Co-PI/ Co-Investigators – Dr. Vidya Arankalle, Dr. Shubham Shrivastava, Dr. Harshad Patil, Dr. Ruta Kulkarni, Dr. Rashmi Virkar. Ph.D. Students: None Human Ethical Approval: IEC/2019/33

Background: Dr Ruta Kulkarni, Dr Rashmi Virkar, and Dr Deepali Mali managed the projects given below (Table 1).

Total tests performed: 8534

Table 1: Details of the testing services provided

Sr. No.	Project Title (Project ID)	Client	Name of test (No. of tests performed)
1.	A Phase II, Single blind, Randomized, Parallel group, Dose ranging, Single Dose Study of Dengue Monoclonal antibody (Dengue mAb) in Adults with Dengue Fever (SII-DEN-mAB)	Serum Institute of India Pvt. Ltd.	DENV PRNT (1948)
2.	A phase I single blind randomized placebo-controlled study to evaluate the safety and immunogenicity of live attenuated tetravalent recombinant dengue vaccine of HBI in healthy adults of 18 to 50 years of age (IIL-DEN)	Abiogenesis Clinpharm Private Ltd.	1. DENV PRNT (1720) 2. DENV serotyping by qRT-PCR (440) 3. DENV quantification by qRT-PCR (19) 4. DENV specific TNF-alpha ELISPOT (258) 5. DENV specific IFN-gamma ELISPOT (258)
3.	Establish serial Sero-Surveillance to monitor the trend of SARS-CoV-2, Dengue and Chikungunya infection transmission in general population India (DRIVEN-2020)	NBM, BIRAC	DENV PRNT (2172)
4.	Neutralization assays (PRNT) to determine persistence of Dengue antibodies in the study (PKC-DEN)	Pune Knowledge Cluster	DENV PRNT (544)
5.	Prospective, multi-center, randomized, open label, active control, phase 2 clinical study to evaluate immunogenicity, safety and tolerability of single heterologous booster dose of RelCoVax® (Protein Subunit Vaccine of Reliance Life Sciences	Reliance Life Sciences	SARS-CoV-2 PRNT (508)

	against SARS-CoV-2 Virus) with Corbevax® (Protein Subunit Vaccine of Biological E Ltd. against SARS-CoV-2 Virus)(RLS-CoV/2023/01)		
6.	A phase, observer- blind, randomized study to assess the safety and immunogenicity of heterologous prime-boost COVID-19 vaccines regimens in individuals aged 18 to 65 years (IVI Korea-CoV)	IVI, Korea	SARS-CoV-2 PRNT (667)

1. A Phase II, Single blind, Randomized, Parallel group, Dose ranging, Single Dose Study of Dengue Monoclonal antibody (Dengue mAb) in Adults with Dengue Fever (SII-DEN-mAB) Serum Institute of India Pvt. Ltd. DENV PRNT (1948)

2. A phase I single blind randomized placebo-controlled study to evaluate the safety and immunogenicity of live attenuated tetravalent recombinant dengue vaccine of HBI in healthy adults of 18 to 50 years of age (IIL-DEN) Abiogenesis Clinpharm Private Ltd. 1. DENV PRNT (1720) 2. DENV serotyping by qRT-PCR (440)
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6. A phase, observer- blind, randomized study to assess the safety and immunogenicity of heterologous prime-boost COVID-19 vaccines regimens in individuals aged 18 to 65 years (IVI Korea-CoV) IVI, Korea SARS-CoV-2 PRNT (667)

2.Title: Platelet-derived exosomes and their role in endothelial dysfunction in dengue infection (Project ID: CD/19/2/E) Funding: Intramural Duration: Mar 2019 – Feb 2022 Sanctioned Amount: Rs. 46.39 Lakhs Investigators: PI – Dr. Shubham Shrivastava, Co-PI/ Co-Investigators – Dr. Vidya A. Arankalle, Dr. A C. Mishra (IRSHA) Ph.D. Student: Ms. Sayali Vedpathak Human Ethical Approval: BVDUMC/IEC/8

Background: This study aimed to evaluate the role of platelet-derived exosomes and exosome-associated microRNAs in the regulation of vascular integrity during dengue infection.

Work done:

1.Dengue virus changes the platelet-derived exosomal miRNA profile:

miRNA profiling was performed using platelet-derived exosomes isolated from mock and dengue virus-exposed platelets. Change in the expression profiles of all the miRNAs inside the exosomes in response to dengue infection was shown by a clustered heat map in Figure 1A. Of 372 miRNAs, the expression of 164 miRNAs was not detectable in platelet-derived exosomes, the remaining detected 208 miRNAs, 59 remained unchanged and 149 miRNAs were significantly dysregulated of which 107 miRNAs were significantly upregulated and 42 miRNAs were downregulated by 2-fold as shown in Figure 1B. This data suggests that dengue infection alters the expression of small non-coding miRNAs in platelet-derived exosomes. The top 10 significantly upregulated and top 10 downregulated miRNAs in platelet-secreted exosomes in response to dengue infection as shown in Figure 1C. The online miRNA target prediction tools, MIENTURNET and Shiny GO 0.80 were used to identify the modulated signaling pathways in response to the top 10 dysregulated miRNAs. The modulated signaling pathways are shown in Figure 1D. Our data indicates that dysregulated miRNAs affect the biological functions of dengue infection.

2. Screening of miRNAs targeting endothelial barrier proteins:

Since, our previous study suggested the role of platelet-derived exosomes in disruption of vascular integrity, we focused on the exosomal-miRNA signature linked with the alteration of six major cell adhesion pathways in dengue infection. A total of 940 genes corresponding to these six cell adhesion pathways were extracted from miRWalk. The top 10 miRNA families affecting genes targeting cell adhesion pathways contain 32 miRNAs and the expression profiles of these 32 miRNAs were matched with profiling data. Of these 32 miRNAs, 16 miRNAs were upregulated at least 5-fold and were pursued further. Of these, 3 miRNAs – miR-27a-3p, miR-29a-3p, and miR-200b-3p targeting genes belonging to at least four cell adhesion pathways were chosen to examine their effect on the integrity of endothelial cells. As the next step, transfection studies will be carried out using HUVEC cells to study the gain or loss of function of the three selected miRNAs.

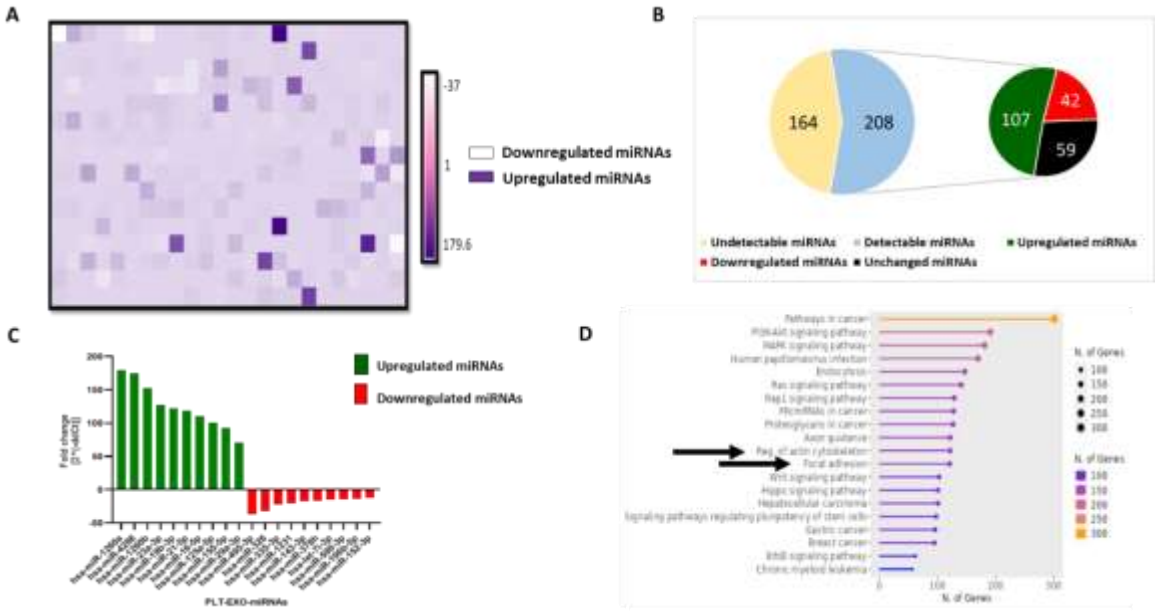

Figure 1. Expression profiles of miRNAs in platelet-derived exosomes. (A) Heatmap of expression profiles of all differentially expressed miRNAs in exosomes isolated from dengue virus-exposed platelets vs mock platelets. (B) Total number of miRNAs expressed in exosomes. (C) Expression profiles of top 10 upregulated and downregulated miRNAs in dengue virus-exposed platelet-derived exosomes. (D) Top 20 signaling pathways targeted by top 10 dysregulated miRNAs.

Conclusion: Dengue infection modulates the expression profiles of miRNA inside the platelet-derived exosomes.

3. **Title: Development and comparative assessment of Antibody-Dependent Enhancement (ADE) assays for dengue viruses (Project ID: CD/23/1/I) Funding: DBT-BIRAC (as part of NIBEC Project CD/19/1/E) Sanctioned Amount: NA Duration: April 2023 – Mar 2025 Investigators: PI - Dr. Shubham Shrivastava; Co-PI/ Co-Investigators - Dr. Vidya A. Arankalle, Dr. A.C. Mishra (IRSHA) Ph.D. Student: Shweta Chelluboina Human Ethical Approval: BVDUMC/IEC/9**

Work done:

1. Optimization of ADE infection assay employing K562 cell lines for the measurement of enhanced viral titers:

The pan-flavivirus cross-reactive mAb 4G2 (HB112) antibody known to enhance dengue virus infection of all four serotypes was used to develop the ADE-infection assay. Different parameters such as cell lines, cell density, hours post-infection, and virus multiplicity of infection were assessed.

Effect of different cell lines

We evaluated antibody-dependent infection enhancement in Fc□RIIa-expressing cells i.e., U937, K562, and Vero-CD32a cells. Vero cells were used as the non-Fc□RIIa expressing cell line (negative control). The peak antibody-dependent enhancement of the DENV-2 virus infection was estimated using different concentrations of HB112 antibody in all four cell lines. The peak enhancing concentration of HB112 was 1µg/ml in both U937 and K562 cells. However, in Vero-CD32a and Vero cells, the virus control wells were fully saturated with infection and the distinction between infection and infection enhancement was unclear (Figure 2A). Based on these observations, K562 and U937 cell lines were pursued for ADE infection assays.

Effect of different cell densities (20,000 cells or 50,000 cells per well)

At 20,000 cells/well seeding density, 10□g/mL of HB112 antibody concentration was required to neutralize the DENV-2 whereas, at 50,000 cells/well seeding density, even 10□g/mL of HB112 antibody concentration was not enough to neutralize the virus. At 20,000 cells/well, peak enhancement was seen only with 1µg/ml of HB112 concentration in both cell lines. The differences between neutralization and enhancement of viral infection were far more evident at 20,000 cells/well. Therefore, the seeding density of 20,000 cells/well was selected for future experiments (Figure 2B).

Effect of incubation time post-infection (24, 48 & 96 hrs)

Here, the DENV-2 virus at MOI 1 was incubated with 1□g/mL of HB112 in U937 and K562 cells, culture supernatants were collected at different hours post-infection. Noticeable differences were observed in plaque size and morphology depending on the incubation days post-infection (Figure 2C). At 24 hours post-infection, the plaque size was distinct and countable. However, as the hours post-infection progressed to 48hrs and 72hrs,

the plaques increased in size and became less distinguishable.

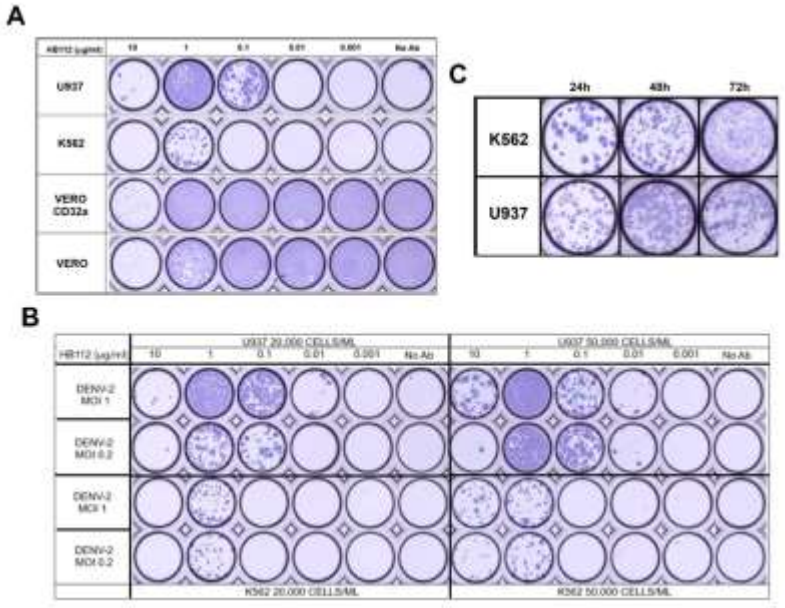

Figure 2. (A) Immunostained DENV-2 plaques from supernatants collected from mixtures of different concentrations of HB112 antibody with DENV-2 virus at MOI 1 incubated with U937, K562, Vero-CD32a, and Vero cells for 24 hours. (B) Comparison of infection enhancement patterns among different cell densities of 20,000 and 50,000 cells/well. Supernatants were collected from mixtures of different concentrations of HB112 antibody with DENV-2 virus at MOI 1 and 0.2 incubated with U937 and K562 cells for 24 hours. (C) Comparison of the plaque morphology at different time points. Supernatants were collected from mixtures of DENV-2 at MOI 1 and 1µg/ml of HB112 incubated with K562 and U937 cells at 24-, 48-, and 72-hours post-infection.

Effect of different input virus multiplicity of infection (MOI)

To check whether the input virus concentration has any effect on the enhancement of infection, serially diluted HB112 antibody was incubated with different MOIs - 5, 1, 0.2, and 0.04 of DENV-2 and 4 viruses. As expected, a higher MOI of virus infection yielded fewer plaques while no plaques were seen at lower MOI in virus-only wells in U937 cells. Very few countable plaques to zero plaques were observed in the virus-only wells at higher and lower MOI in K562 cells. This further validates the lower susceptibility of U937 and K562 cells over Vero and Vero-CD32a cells. The enhancement of infection was only seen with virus-antibody complexes due to the presence of Fc□RIIa on these cells. The peak enhancement was seen at 0.5 and 5µg/ml concentrations of HB112 antibody at different MOIs of DENV-2 virus in U937 and K562 cells respectively. The degree of enhancement was much higher in K562 than in U937 cells at 1 and 0.2 MOIs of DENV-2 virus with 0.5µg/ml of HB112 antibody (Figure 3A, B).

For the DENV-4 virus, peak enhancement of infection was seen at the HB112 antibody concentrations of 5 µg/ml in both U937 and K562 cells. In K562 cells, 50 µg/ml of HB112 did not efficiently neutralize the DENV-4 virus at different MOIs. Like DENV-2, the degree of enhancement of DENV-4 infection was higher in K562 than in U937 cells even at lower MOIs (Figure 3C, D).

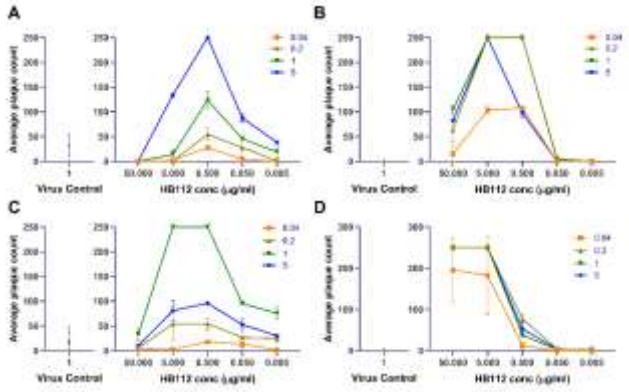

Figure 3. A plot of average plaque counts across concentrations of HB112 at different MOI of DENV-2 and DENV-4 virus in both U937 and K562 cells. A virus control panel indicates the number of plaques obtained in virus control wells without any antibody mixture in respective cells. The top panel indicates DENV-2 virus infection enhancement in (A) U937 and (B) K562 cells whereas the bottom panel indicates DENV-4 virus infection enhancement in (C) U937 and (D) K562 cells.

2. ADE infection assay using healthy blood donor samples:

The optimized ADE assay in U937 and K562 cells was used to screen twelve healthy blood donor samples at MOI 1 in U937 cells and MOI 0.2 in K562 cells. All nine anti-dengue IgG positive samples showed enhancement of infection at a particular dilution, and all three anti-dengue IgG negative samples showed no enhancement of infection of DENV-2 and 4 viruses in both U937 and K562 cells. 3/9 (33%) of healthy donor samples showed peak fold enhancement of infection at 1:200 dilution and 1:2000 dilution for DENV-2 and DENV-4 viruses respectively in U937 cells (Figure 4A-B). Similarly, 4/9 (44%) and 3/9 (33%) healthy donor samples showed peak fold enhancement of infection at 1:2000 dilution for DENV-2 and DENV-4 virus respectively in K562 cells (Figure 4C-D). We plotted the graph of fold-infection enhancement to understand the magnitude of the enhancement of infection. The fold-infection enhancement for DENV-2 virus was comparable in the two cell lines ($p = 0.062$, Figure 4E). The fold-infection enhancement for the DENV-4 virus was significantly higher in K562 than U937 cells ($p < 0.01$, Figure 4F).

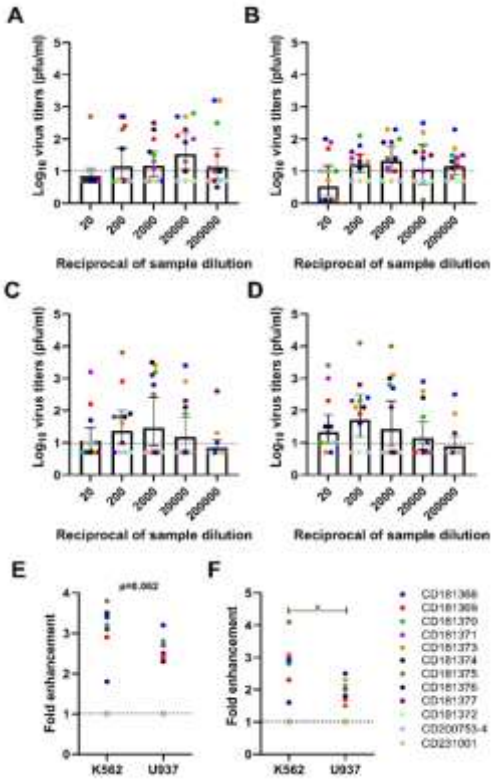

Figure 4. A scatter plot of log10 virus titers (pfu/ml) at different dilutions (1:20 to 1:20,000) of 12 healthy donor samples. Data is presented as geometric mean titers with 95% CI as error bars. The enhancement of infection for (a) DENV2 and (b) DENV-4 viruses was observed in U937 cells. The enhancement of infection for (c) DENV2 and (d) DENV-4 viruses was observed in K562 cells. The dotted line indicates the cut-off value for fold enhancement at different dilutions. The virus titer at different sample dilutions was normalized by the average virus titer in virus-only wells. A dot plot of the magnitude of fold enhancement in terms of virus titers, pfu/ml among 12 healthy donor samples for (e) DENV-2 and (f) DENV-4 viruses in K562 and U937 cells. A baseline was drawn at mean values from 3 IgG negative samples (dotted line). Wilcoxon-signed rank test was used for paired analyses. *indicates p-value <0.01.

Our data suggests a higher and more prominent enhancement of infection in K562 cells for both DENV-2 and DENV-4 viruses. Also, there were zero plaques in virus control of K562 cells which is indeed an ideal scenario that no virus should replicate in the absence of antibodies in immune cells as opposed to countable plaques seen in U937 cells.

Conclusions:

1. ADE infection assay employing the K562 cell line is the most appropriate cell line for studying infection enhancement in samples.
2. 100% of anti-dengue IgG-positive samples showed infection enhancement at sub-neutralizing dilution.

4.Title: Development of immunostaining-based microneutralization test for chikungunya viruses (Project ID: CD/23/2/I) Funding: DBT-BIRAC (as part of NIBEC Project CD/19/1/E) Sanctioned Amount: NA, Duration: April 2023 – Mar 2024 Investigators: PI - Dr. Shubham Shrivastava; Co-PI/ Co-Investigators - Dr. V A Arankalle, Dr. A.C. Mishra Human Ethical Approval: NA

Background: We have a standardized, validated, and NABL-accredited plaque reduction neutralization test (PRNT) based on crystal violet staining in a 24-well format. The necessity of standardization of a test amicable for automation and possibly with enhanced sensitivity was considered essential.

Objective: To improve the sensitivity of chikungunya-PRNT by using immunostaining in a 96-well format i.e. micro-FRNT.

Work done: For the development of an immunostaining-based micro-FRNT, the following cell culture conditions and parameters were optimized:

1.Incubation time post-infection

2.Overlay media concentration

3.Input virus concentration

4.Incubation time for virus adsorption during infection

Anti-CHIKV neutralizing antibody titers were compared by testing 10 serum samples positive for IgG-anti-CHIKV antibodies (Table 2). The average titers in µFRNT50 were 3.3-fold higher than the standard PRNT50. When 123 samples were subjected to both tests, 24 were negative and 51 scored reactive on both tests. However, micro-FRNT could detect neutralizing antibodies in 48 additional samples increasing positivity from 41.5% (PRNT) to 80.5% in the micro-FRNT. The average µFRNT50 titers were 2.7-fold higher than the standard PRNT50 titers, suggesting that the sensitivity of µFRNT is higher than the PRNT.

Table 2. Comparison of anti-CHIKV neutralizing antibody titers by two methods

Sample ID	Std $PRNT_{50}$	$\mu FRNT_{50}$	Fold diff.
CD181370	804	2805	3.5
CD181371	465	2260	4.9
CD181375	117	283	2.4
CD230023	1312	4738	3.6
CD230044	1226	3806	3.1
CD170046-9	1730	3284	1.9
CD230061	527	1995	3.8
CD230064	474	1608	3.4
CD230253	1858	7161	3.9
CD170045-8	2144	6546	3.1
PC01122018	421	1876	4.5

Mean titers*	1007	3306	3.3

*p-value=0.0005

The micro-FRNT was validated as per ICH Q2 (R2) guidelines and parameters such as Accuracy, Precision, and Quantitation limits were evaluated.

Conclusion: CHIKV-specific immunostaining-based microneutralization test is superior to standard PRNT. A validated test is now available.

5.Title: Development of potent adjuvanted respiratory syncytial virus vaccine for mucosal delivery (Project ID: CD/19/3/E) Funding: Wellcome-DBT India Alliance Duration: January 2019 - December 2023 Sanctioned Amount: 1.69 crore Investigators – PI - Dr. Harshad Padmanabh Patil, Co-PI/ Co-Investigators - Dr. Vidya Arankalle Ph.D. Student: Mr. Ahmedali Mandviwala Animal Ethical Approval: BVDUMC/1881/2018/002/010 (renewed number BVDUMC/819/2022/002/017)

Background: The study plans to evaluate the immunogenicity of adjuvanted, RSV-virus-like-particles (RSV-VLPs)-based vaccine administered by mucosal route, in mice. The chimeric adjuvants used are recognized by two PRR ligands. During the previous years, RSV-VLPs were developed and immunogenicity of unadjuvanted RSV-VLPs was evaluated by intramuscular route.

Objectives:

1. Production of candidate RSV vaccines, consisting of VLPs and different combinations of adjuvants
2. Determination of the immunological and protective properties of these vaccine candidates in mice
3. Evaluation of the effects of these vaccine candidates on human PBMCs or PBMC-derived cells

Work done: Work on objective 2 was executed in the year. Two delivery routes, i.e., pulmonary and intranasal were evaluated. Pulmonary delivery:

1. IgA response in the nasal cavity: IgA in the nasal cavity is shown to be associated with protection at the mucosal surfaces. Therefore, the induction of IgA antibodies by the adjuvanted RSV-VLPs after pulmonary immunization in the nasal cavity was evaluated (Figure 5 1a-c). Only mice immunized with CL413 adjuvanted VLPs induced significantly

higher IgA levels against VLPs, preFg, and, G proteins. No IgA induction was observed when only VLPs or VLPs adjuvanted with Pam3CSK4+L18-MDP, Pam3CSK4+IMQ, or CL429 were administered in mice. Notably, IgG-anti-RSV was not detected in the nasal cavity after pulmonary immunization (data not shown).

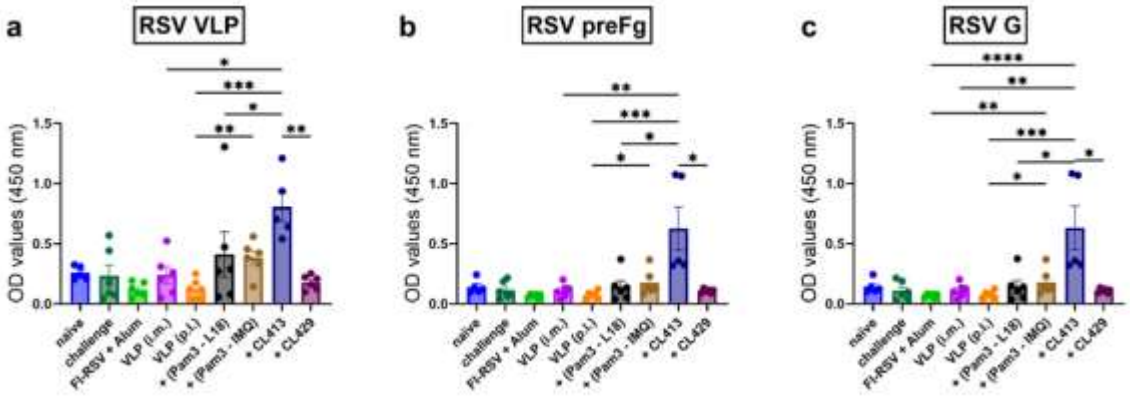

Figure 5. Antibody response in the nasal cavity. Immunized mice were sacrificed four days after the challenge with live RSV. The nasal cavity was flushed with 1 ml PBS containing protease inhibitor. Undiluted nose wash was added directly to coated plates with purified VLPs or ExpiSF9 cell supernatant containing RSV preFg or G proteins. ELISA was performed to determine IgA antibodies against (a) VLPs, (b) preFg and (c) G proteins. Statistical analysis was accomplished by using a one-way ANOVA tes : *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$

2. Systemic humoral immune response: To understand the systemic antibody generated after immunization with adjuvanted-VLPs via the pulmonary route, binding IgG antibody levels (Figure 6 a-c) against preFg, G, M; and RSV-neutralizing antibody levels (Figure 6d) were measured in serum samples obtained post-second dose. Except for the CL413 adjuvanted-VLPs, all other formulations induced similar levels of IgG as those induced after pulmonary delivery of unadjuvanted VLPs. CL413 adjuvanted VLPs and alum-adjuvanted FI-RSV induced comparable IgG levels. Importantly, the IgG levels were not lower than those induced after intramuscular delivery of the VLPs. All the immunized mice induced neutralizing antibodies (Figure 6d), however, the levels induced by pulmonary immunized, adjuvanted groups were lower than intramuscularly immunized mice.

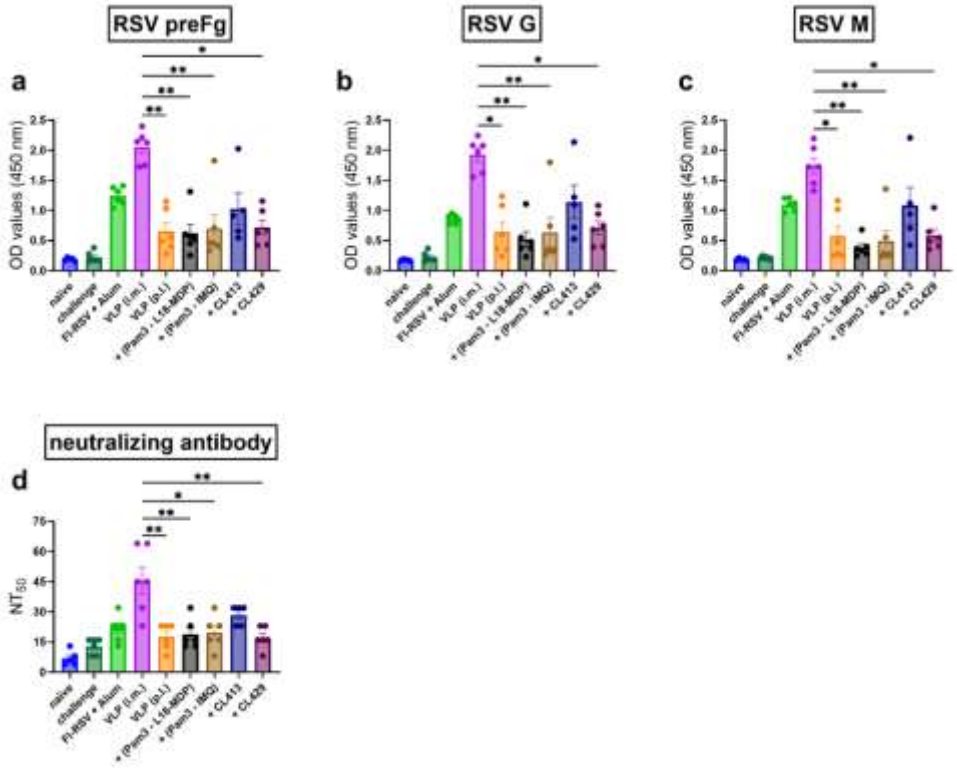

Figure 6. Systemic humoral immune response after immunization. Immunized mice were challenged with live RSV and sacrificed four days post-challenge. Blood was collected during the sacrifice and humoral response was determined by measuring IgG-anti (a) -preFg protein (b) -G protein, (c) -M protein by ELISA and (d) neutralizing antibodies employing Hep-2 cells. Statistical analysis was accomplished by using one-way ANOVA test: *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; ****, $p < 0.0001$.

3. Inflammatory and anti-inflammatory cytokine response in lungs and spleens: Cytokines play a key role in shaping the immune response by secretion of various cytokines in response to RSV infection. We next evaluated the antigen-specific inflammatory (Figure 7a-j) and anti-inflammatory (Figure 7k-n) cytokine responses after in vitro stimulation of the lung lymphocytes and splenocytes from the immunized mice.

Mice immunized with VLPs by intramuscular route failed to elicit antigen-specific pro-inflammatory cytokines in the lungs. The release of a few cytokines at minimal levels was observed in mice immunized with FI-RSV. VLP+CL413 induced the highest levels of the pro-inflammatory cytokines in the lungs (Figure 7a-e). Pam3+IMQ-adjuvanted VLPs also induced pro-inflammatory cytokines but only IFN-γ levels were equivalent to that elicited by VLPs+CL413. VLP adjuvanted with Pam3+L18-MDP induced all the evaluated pro-inflammatory cytokines, except IL-6, in the lungs. Immunization with VLP+CL429 elicited minimal levels of all the pro-inflammatory cytokines in the lungs.

Analysis of anti-inflammatory cytokines from the lung cells highlighted that the mice immunized with FI-RSV produced about 30-fold more IL-4 (Figure 7k) when compared to

pulmonary delivery. Although no difference was seen in IL-10 levels (Figure 7m) between FI-RSV and adjuvanted VLPs-immunized mice.Delivery of un-adjuvanted VLPs by intramuscular or pulmonary routes produced 2-3 fold more IL-10 than the other groups.

Next, we compared secretion of cytokines by the stimulated splenocytes in the culture supernatants. TNFα levels were independent of the delivery route of the VLPs (Figure 7g). The levels of pro-inflammatory cytokines IFN-γ (Figure 7f) and IL-6 (Figure 7h) and anti-inflammatory cytokines IL-4 (Figure 7m) and IL-10 (Figure 7n) were higher in intramuscularly immunized mice. Surprisingly, IL-2 (Figure 7i) and IL-17A (Figure 7j) levels were highest in the mice immunized by VLPs+CL413 by pulmonary route.

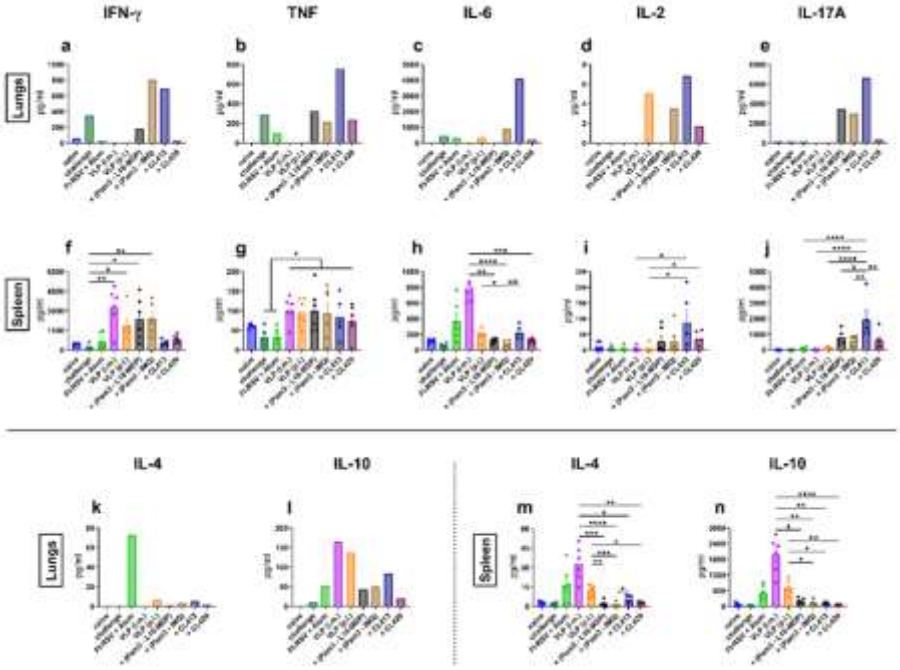

Figure 7. Inflammatory and anti-inflammatory cytokine responses after immunization. Mice were sacrificed 4 days after challenge following the second immunization dose. Lung lymphocytes from one group were pooled and used for the assay. Splenocytes from each mouse were cultured separately. The cells were cultured either in the presence or absence of purified VLPs for 18hrs. Supernatants were used to determine (a & f) IFN-γ, (b & g) TNFα, (c & h) IL-6, (d & i) IL-2, (e & j) IL-17A, (k & i) IL-4 and (m & n) IL-10 from non-stimulated and stimulated cells employing cytometric bead assay. Antigen specific response was determined by subtracting values of the cytokines of non-stimulated cells from the stimulated cells. Statistical analysis was accomplished by using the non-parametric Kruskal-Wallis test: *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$.

4. Protection from RSV after challenge: To investigate whether mucosal delivery of RSV-VLPs protects the mice from RSV-induced lung pathology, we examined the lungs from the RSV-challenged mice one week post second immunization. (Figures 8a-i). No lung pathology was observed in mice immunized by intramuscular route. Importantly, the signs

of alveolitis and infiltrates in bronchial and vascular areas were not observed in the mice immunized with unadjuvanted or adjuvanted VLPs by pulmonary route (Figure 8j).

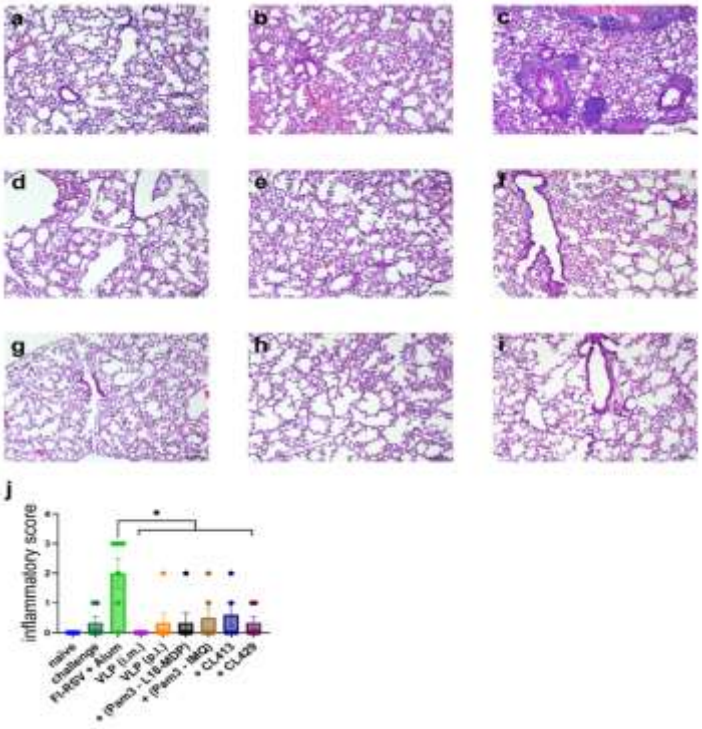

Figure 8. Protection from lung pathology after immunization and RSV challenge. Immunized mice were challenged with wild type-live RSV and lungs were harvested 4 days after challenge. Lungs were fixed, sectioned, and stained with H&E to evaluate RSV-mediated respiratory disease. Representative images of the H&E-stained lung sections from (a) naïve, (b) non-immunized and challenged (c) FI-RSV + alum immunized (d) intramuscularly administered VLP, pulmonary administered (e) VLP, (f) VLP+Pam3CSK4+L18-MDP (g) VLP+Pam3CSK4+imiquomode, (h) VLP+CL413 and (g) VLP+CL429 mice. The lung pathology score was calculated after analyzing the lung sections from each mouse. Statistical analysis was accomplished by using the non-parametric Kruskal-Wallis test: *, $p < 0.05$.

Intramuscular delivery:

1. Systemic humoral immune response after immunization of adjuvanted-VLPs by intramuscular route: To determine the relative efficacy of the RSV-VLPs combined with different adjuvants, mice were immunized twice at 3-weeks interval via the intramuscular route. RSV-binding IgG antibody levels (Figure. 9a-d) and RSV-neutralizing antibody levels (Figure 9e) were measured in sera collected post second dose. The immune response elicited by FI-RSV (adjuvanted with Alum) and the unadjuvanted VLPs were the comparators. Beneficial effect of adjuvantation was not seen on total binding IgG response against the VLPs (Figure 9a). However enhanced antibody induction against preF and M,

was seen when VLPs were administered with CL413 (Figure 9b-d). All the adjuvant-VLP immunized mice induced higher levels of neutralizing antibodies compared to the unadjuvanted VLPs or the alum-adjuvanted FI-RSV (Figure 9e).

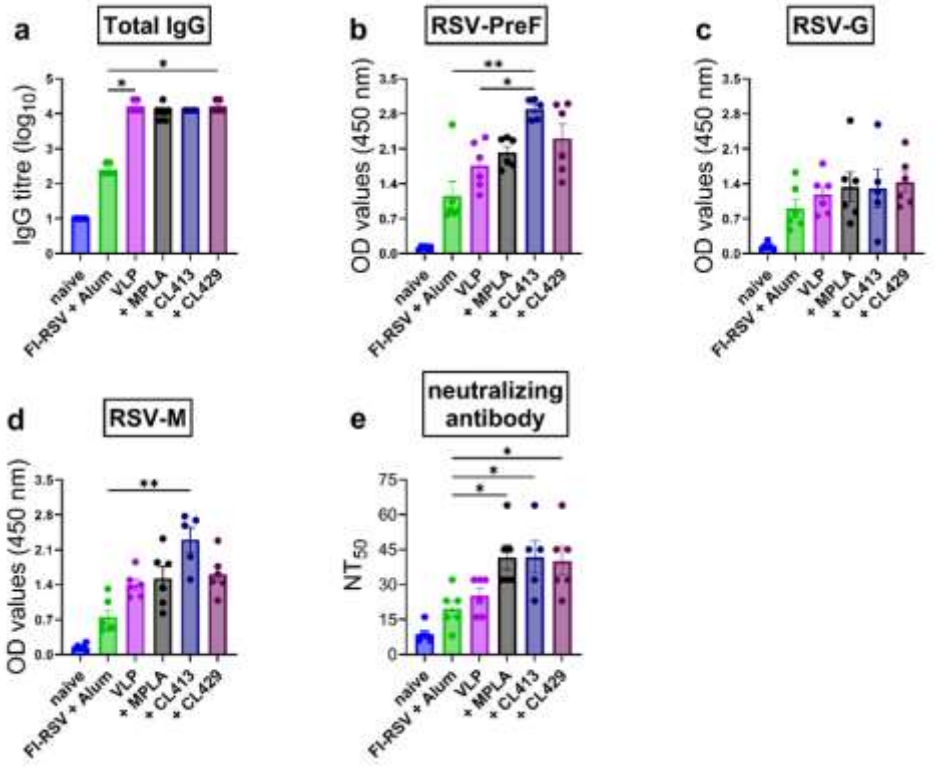

Figure 9. Systemic humoral immune response after immunization. Mice were left untreated (naïve) or were immunized twice on day 1 and day 21 with 5 µg of alum adjuvanted FI-RSV or 5 µg of unadjuvanted RSV-VLPs or 5 µg RSV-VLPs combined with 20 µg each of MPLA, CL413 and CL429 adjuvants via the intramuscular route. Sera was collected seven days post second dose (day 28). Humoral responses after immunization were determined by measuring (a) total IgG-anti-RSV antibody titer against RSV, ELISA reactivity of the collected sera against (b) RSV-preF, (c) RSV-G and (d) RSV-M proteins and (e) RSV neutralizing antibody titers. Statistical analysis was accomplished by using the non-parametric Kruskal-Wallis test: *, $p < 0.05$; **, $p < 0.01$. Bar represents mean ± SEM.

2. Inflammatory and anti-inflammatory cytokine response after immunization: We next evaluated the inflammatory (Figure. 10a-e) and anti-inflammatory (Figure. 10f and g) cytokine responses after in vitro stimulation of the splenocytes harvested from the immunized and challenged mice. Overall, immunization with VLP+CL413 induced moderately higher levels of pro-inflammatory cytokines TNFa (p=0.16, Figure. 10b), IL-6 (p=0.32, Figure. 10c) and IL-2 (p=0.24, Figure. 10d) compared to the unadjuvanted or MPLA and CL429 adjuvanted VLPs. Only adjuvantation with CL429 had significant effect on secretion of IFN-γ when compared to the unadjuvanted VLPs (p 0.16, Figure. 10a). Secretion of IL-17A after in vitro stimulation of the splenocytes was seen only in the group

that received VLPs+CL413 (Figure. 10e). Analysis of anti-inflammatory cytokines highlighted MPLA, CL413 and CL429 reduced IL-4 production as compared to the alum adjuvanted FI-RSV (Figure. 10f). No difference was observed in the secreted IL-10 levels between the FI-RSV, unadjuvanted VLP and CL413-VLP immunized mice. A 2-fold decrease in IL-10 levels in the MPLA or CL429 immunized mice were also observed (Figure. 10g).

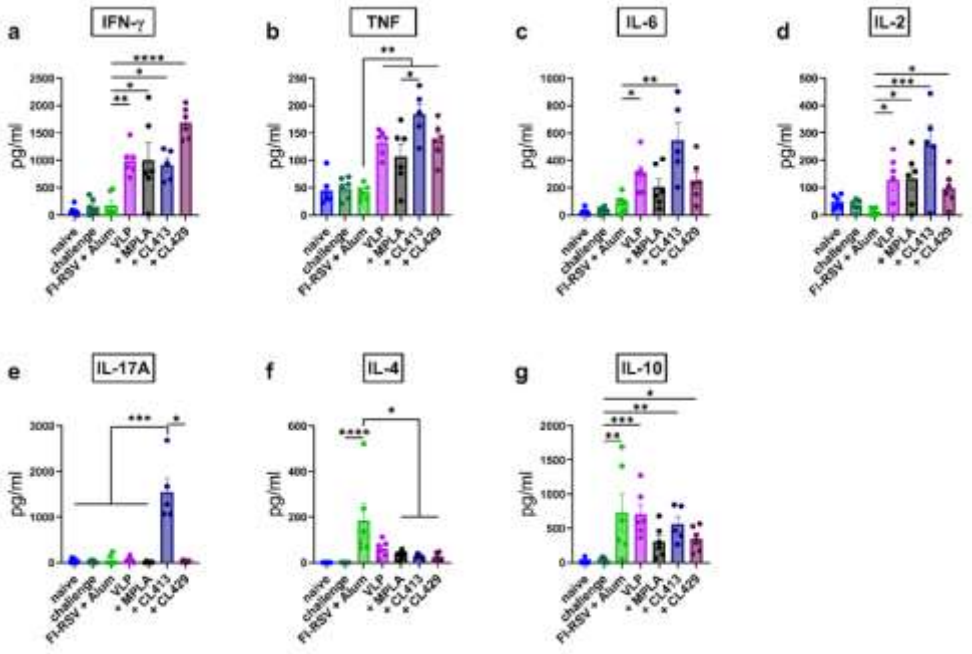

Figure 10. Inflammatory and anti-inflammatory cytokine responses after immunization. Mice were sacrificed 4 days after challenge with wild-type RSV immunization (day32). Individual spleens from each mouse were processed and splenocytes were cultured either in presence or absence of RSV-VLP stimuli. Antigen-specific release of cytokines - (a) IFN-γ, (b) TNF, (c) IL-6, (d) IL-2, (e) IL-17A, (f) IL-4 and (g) IL-10 were determined by subtracting values of the cytokines of non-stimulated cells from the stimulated cells for each mouse. Statistical analysis was accomplished by using the non-parametric Kruskal-Wallis test: *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; ****, $p < 0.0001$. Bar represents mean ± SEM.

3. Protection of immunized mice after RSV challenge: To investigate whether intramuscular delivery of RSV-VLPs combined with adjuvants protects the mice from RSV induced lung pathology, we examined lungs from mice that were challenged with RSV one week post second immunization (Figure. 11a-g). Mice immunized by unadjuvanted or adjuvanted VLPs by the intramuscular route did not show any signs of alveolitis and infiltrates in bronchial and vascular areas (Figure. 11d-g), compared to the non-immunized challenged mice (Figure. 11b) or the mice immunized with alum adjuvanted FI-RSV (Figure. 11c). The lung pathology score was comparable to the non-challenged mice (Figure. 11a).

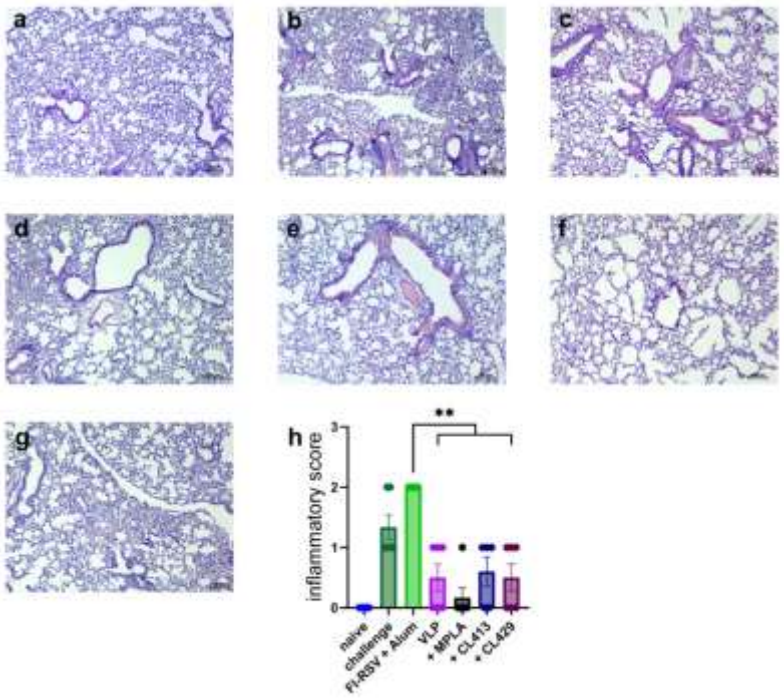

Figure 11. Protection from lung pathology after immunization and RSV challenge. Immunized mice were challenged with wild type-live RSV and lungs were harvested 4 days after challenge. Lungs were fixed, sectioned, and stained with H&E to evaluate RSV-mediated respiratory disease. Representative images of the H&E-stained lung sections from (a) naïve mice, (b) non-immunized and challenged mice, (c) intramuscularly administered alum-adjuvanted FI-RSV, (d) intramuscularly administered unadjuvanted VLPs and VLPs adjuvanted with (e) MPLA (f) CL413 and (g) CL429 mice. (h) The lung pathology score was calculated after analyzing the lung sections from each mouse. Statistical analysis was accomplished by using the non-parametric Kruskal-Wallis test: *, $p < 0.05$; **, $p < 0.01$. Bar represents mean ± SEM.

Conclusions:

1. Among the chimeric adjuvants evaluated, CL413 emerged as a promising mucosal adjuvant for use with the RSV-VLPs. It could enhance nasal IgA, cytokine response in the lungs and effectively modulate systemic response.
2. Limited effect of adjuvantation was observed after intramuscular delivery on antibody response. CL413 enhanced cytokine response towards the antigen.

6.Title: Mucosal IgA response against wild-type SARS-CoV-2 virus and Kappa, Delta, Omicron variants during three disease waves in Pune, India. (Project ID: CD/23/3/I) Funding: DBT-BIRAC (as part of NIBEC Project CD/19/1/E and CD/21/1/E) Duration: July 2023- October 2023 Sanctioned Amount: NA Investigators: PI - Dr. Vidya A. Arankalle; Co-PI/ Co-Investigators - Dr. Rashmi Virkar, Dr. A.C. Mishra.Ph.D. Students: NA Human Ethical Approval: IEC/2020/25

Background: Mucosal-IgA plays a vital role as the first line of defense against respiratory viruses, however limited studies address mucosal IgA (sIgA) responses against SARS-CoV-2 during different disease waves caused by different variants.

Objectives:

1. To evaluate SARS-CoV-2 sIgA response among the COVID-19 patients representing three disease waves, using inactivated wild virus-based ELISA.
2. To evaluate SARS-CoV-2 sIgA response and cross-reactivity among the above-mentioned patients using wild-type, Delta, Kappa and Omicron RBD protein-based ELISAs.

Work done: An inactivated virus-based ELISA and recombinant RBD protein-based ELISAs were standardized. Homologous and cross reactive sIgA-anti-SARS-CoV-2 antibody responses were analysed using nasopharyngeal swab samples (n=627) from SARS-CoV-2 infected patients from all three waves (Figure. 12). The inactivated virus-based ELISA was highly sensitive and specific with 96% sensitivity and 86% specificity. We showed that 90-99% of nasopharyngeal swab samples were sIgA positive at diagnosis during the three disease waves (Figure. 13). Viral load was inversely proportional to sIgA levels. Irrespective of the use of inactivated virus/RBD ELISAs, sIgA-anti Kappa and sIgA-anti-Omicron levels were lower. Though the degree was variable, cross-reactivity between all the RBDs was noteworthy. The mutations in the infecting variant influenced IgA reactivity. When sIgA levels among wild-type and breakthrough infections with kappa/delta/omicron variants were tested with all the 4RBDs, the "Immune imprinting phenomenon" was apparent. Our results provide insight into the sIgA response during the three pandemic waves in India.

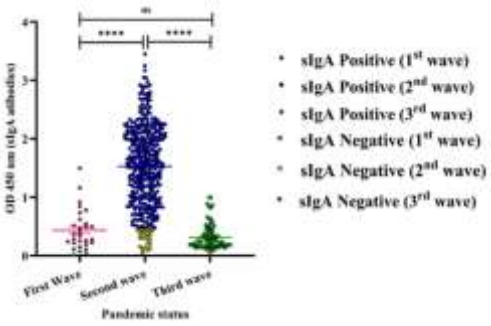

Figure 12. An inactivated virus-based ELISA based evaluation of sIgA (mucosal) immune responses during three pandemic waves in India.

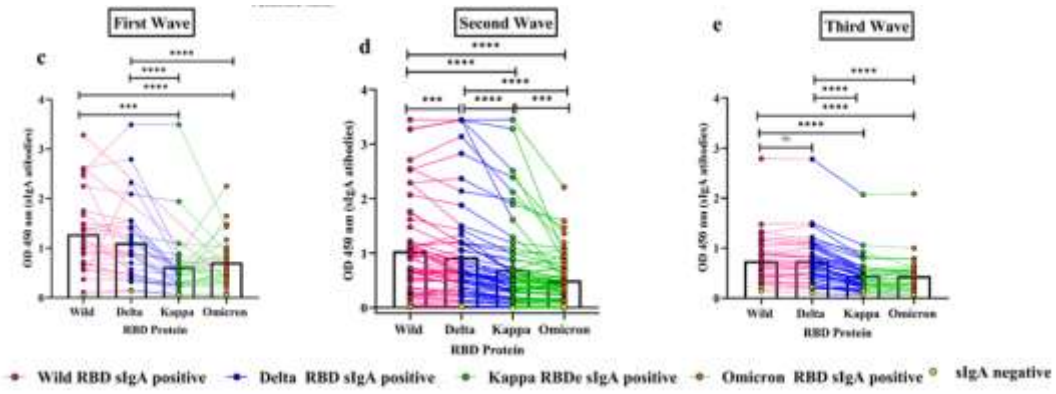

Figure 13. Recombinant RBD protein-based ELISA-based evaluation of sIgA (mucosal) immune responses during three pandemic waves, a) First Wave, b) Second Wave, and c) Third Wave in India.

Conclusions:

1 An inactivated virus-based ELISA for detecting sIgA-anti-SARS-CoV-2 antibodies was standardized with 96% sensitivity and 86% specificity.

2 Viral load was inversely proportional to sIgA levels and mutations in the infecting variant influenced the sIgA reactivity.

7.Title: Evaluation of antibody response against SARS-CoV-2 Omicron BA.5 and Xbb variants and comparison of these responses with earlier evaluated response against Wild, Delta, Kappa and Omicron BA.1 variants among SARS -CoV-2 convalescent and vaccinated subjects. (Project ID: CD/23/4/I); Funding: Intramural Sanctioned Amount: NA Duration: July 2023– June 2024 Investigators: PI - Dr. Vidya A. Arankalle; Co-PI/ Co-Investigators - Dr. Rashmi Virkar Ph.D. Students: NA Human Ethical Approval: BVDUMC/IEC/71, BVDUMC/IEC/185A

Background: Unprecedented spread of SARS-CoV-2 with upsurging of new Omicron sub-variants led to evolution of new sub-variants Omicron BA.5 and Xbb 1.16. Earlier we have evaluated neutralizing antibody responses against Wild, Delta, Kappa and Omicron viruses.

Work done: This study is extension of that study where responses against BA.5 and Xbb 1.16 were evaluated and compared with already evaluated responses. This study was conducted both in convalescent subjects and Covishield and Covaxin recipients. When compared with Kappa, Delta, and Omicron (BA.1, BA.5, and Xbb 1.16) variants, we noted significantly high titers against wild virus than all other variants (Figure. 14). When the response among convalescent subjects and Covishield or Covaxin recipients was compared, it was found that with few exceptions, response was higher in Covishield recipients for wild virus and variants (Figure. 15). We also noted that vaccine recipients

with prior infection had significantly high titre against all the variants (Figure. 16), indicating importance of hybrid immunity.

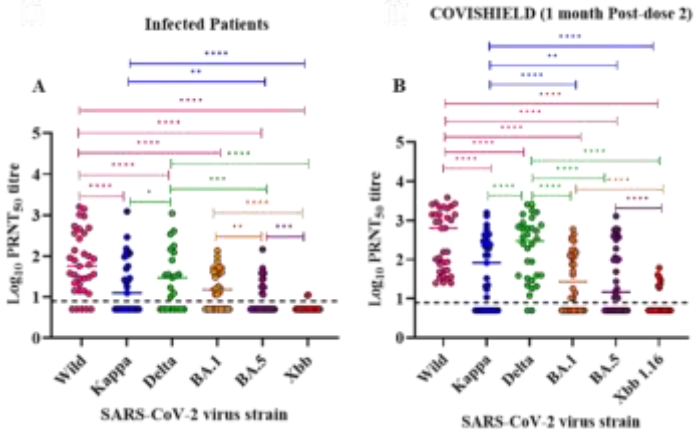

Figure 14. Neutralizing antibody response against SARS-CoV-2 Wild virus and Kappa, Delta, and Omicron variants in (A) infected patients, and (B) vaccinated individuals.

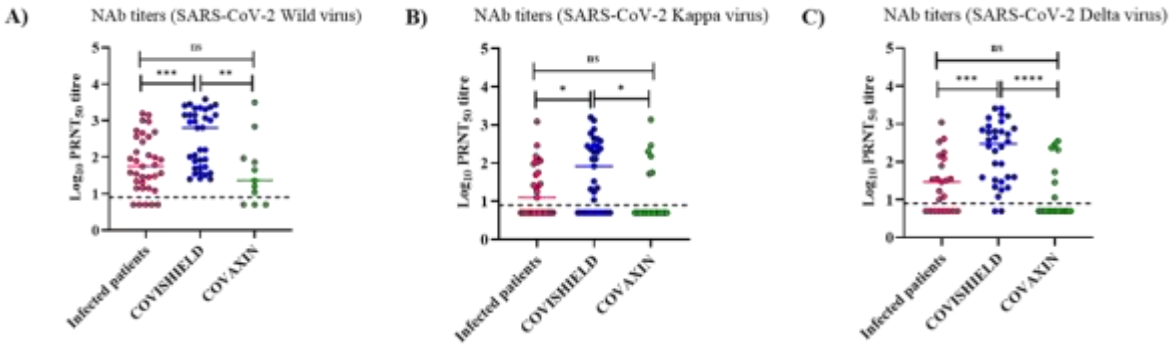

Figure 15. Comparison of neutralizing antibody response against SARS-CoV-2 Wild virus and Kappa, Delta, and Omicron variants among the convalescent subjects and Covishield or Covaxin recipients.

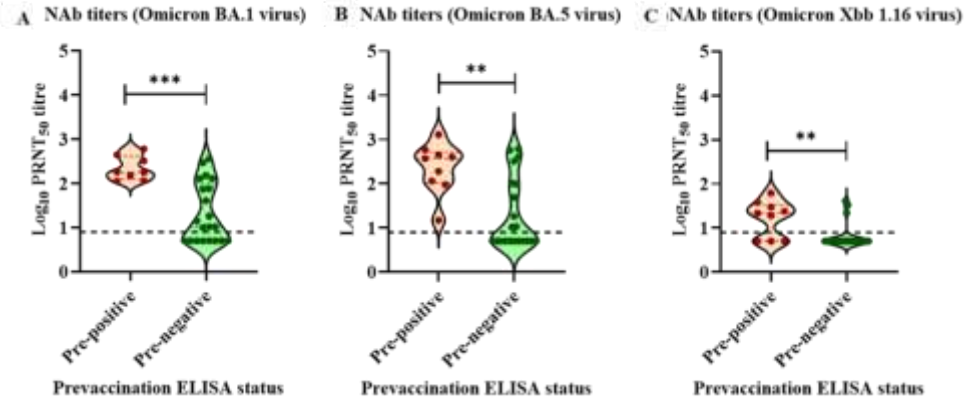

Figure 16. Impact of prior SARS-CoV-2 infection on vaccine responses against A) BA.1 Omicron virus, B) BA.5 omicron and C) Xbb 1.16 Omicron virus.

Conclusions:

1 Covishield vaccine recipients had high antibody titers than in convalescent subjects or Covaxin recipients.

2 Prior exposure to SARS-Cov-2 virus led to enhanced antibody response as seen by high antibody titers among the pre-positives than pre-negative subjects.

8.Title: Evaluation of the antiviral potential of Ribavirin against Dengue virus. (Project ID: CD/23/5/I) Funding: Intramural Sanctioned Amount: NA Duration: July 2023 – August 2023 Investigators: PI - Dr. Rashmi Virkar. Ph.D. Students: NA Human Ethical Approval: NA

Background: Ribavirin is an antiviral medication historically used to treat hepatitis C and RSV. Ribavirin is a guanosine (ribonucleic) analog used to stop viral RNA synthesis and the viral mRNA capping; thus, it is a nucleoside analog. Ribavirin interferes with RNA metabolism required for viral replication and is expected to pose broad anti-viral potency. Dengue being single-stranded positive-sense RNA could be susceptible to Ribavirin, but this remains unexplored. Therefore, we evaluated the anti-viral efficacy of Ribavirin against all Dengue virus serotypes isolated at our lab.

Objectives:

1. Development of the Immuno Detection Assay (IDA)-based platform to evaluate anti-viral drugs against Dengue Viruses.
2. Evaluate the anti-viral efficacy of Ribavirin against all Dengue virus serotypes employing Immuno Detection Assay (IDA).

Work done:

1. Development of Immuno Detection Assay (IDA) based platform:

IDA is performed to quantify a virus using virus-specific antibodies that detect the viral antigen. To standardize Dengue-specific IDA, the Dengue-2 virus was isolated and characterized at IRSHA, and pan-flavivirus-specific HB-112 monoclonal antibodies were used. Vero cells were infected with serially diluted Dengue virus for 24 or 48 hours followed by fixation and permeabilization. A primary antibody (HB-112) was added followed by a goat-anti-mouse-IgG-HRP conjugate. The antigen-antibody complex was detected using Tetramethyl benzidine (TMB) substrate and the reaction was stopped using 2N H_2SO_4. Absorbance was measured at 450 nm.

As virus titers obtained by plaque assay/NS1 ELISA-based assay (3 X 105 TCID50/ml) and by IDA terminated 48 hours post-infection were comparable (3.16 X 105 TCID50/ml), this assay was used for further experiments. Similar conditions were determined for the remaining three serotypes.

2. Evaluation of anti-viral efficacy of Ribavirin against all Dengue virus serotypes employing IDA: The anti-viral efficacy of Ribavirin was evaluated in four stages.

- Determination of cytotoxicity of Ribavirin
- Determination of optimum virus input for infection for anti-viral assessment
- Antiviral assays in Therapeutic, Virucidal, and Prophylactic modes

Based on CC50, different concentrations of ribavirin were used and tested in Prophylactic (Host cell pretreatment for 1, 2, 24 hours), Therapeutic (Post-infection treatment for 1,2,4 hour), or Virucidal (Co-treatment of the virus and ribavirin). Infectivity was evaluated by performing IDA-based virus detection. Ribavirin was found to be a potent therapeutic antiviral drug as evidenced by ≥80% protection against Dengue-1, Dengue-2, and Dengue-4 and ≥ 75% against Dengue-3 at tested time points. Virus infected untreated cells were included as a negative control whereas uninfected and untreated cell control were included as a positive control in the assay.

The percentage CPE inhibition was calculated using the formula:

percentage CPE inhibition = (OD of drug-treated cells − OD of negative control)/(OD of positive control − OD of negative control) × 100

Ribavirin exhibited virucidal activity yielding 58% protection against Dengue-1, 78% against Dengue-2, 64% against Dengue-3, and 56% against Dengue-4 at 2 hours co-incubation). However, no / very low prophylactic activity of Ribavirin was noted against all the vial serotypes when incubated for 2 hours.

Conclusion: Ribavirin demonstrated the highest therapeutic antiviral activity and substantial virucidal antiviral activity against all four dengue serotypes.

9. Title: Isolation and characterization of SARS-CoV-2 Omicron viruses. (Project ID: CD/23/6/I) Funding: Intramural (as part of NIBEC Project CD/19/1/E and CD/21/1/E) Duration: July 2023-June 2024 Sanctioned Amount: NA Investigators: PI - Dr. Vidya A. Arankalle; Co-PI/ Co-Investigators: Dr. Rashmi Virkar, Dr. A.C. Mishra. Ph.D. Students: NA Human Ethical Approval: IEC/2020/25

Background: The pandemic caused by SARs-CoV-2 is characterized by the emergence of variants globally, some restricting to the same area while the others causing waves of the pandemic. We continued our efforts to isolate the variants as the pandemic progressed (Figure 17).

Figure 17. A timeline describing the origin of SARS-CoV-2 Omicron sub-variants during 2023-2024.

Work done: This year was marked by a continued "third wave" caused by newer Omicron subvariants. We isolated the viruses in VERO cells and characterized them by full genome sequencing. Table 3 describes the classification of the subvariants.

Table 3. Classification of Omicron subvariants isolated during 2023-24.

Sr. No.	Isolate ID	Lineage (Pangolin v3.1.7)
1	CD/23/02011	XBB.1.16 [Omicron (BA.2- like)]
2	CD/23/2009	XBB.1.16 [Omicron (BA.2- like)]
3	CD/23/3002	XBB.1.16 [Omicron (BA.2- like)]
4	CD/24/0004	BA.2.86
5	CD/24/0005	BA.2.86
6	CD/24/0006	BA.2.86

Conclusion: We have successfully isolated and characterized three isolates each of BA 2.86 and Xbb1.16 SARS-CoV-2 variant.

10.Title: Development of variant-specific Plaque Reduction Neutralization (PRNT) and micro-PRNTs to assess neutralizing antibody response. (Project ID: CD/23/7/I) Funding: Intramural (as part of NIBEC Project CD/19/1/E and CD/21/1/E) Duration: July 2023– November 2023 Sanctioned Amount: NA Investigators: PI - Dr. Rashmi Virkar; Co-PI/ Co-Investigators: Dr. Vidya A. Arankalle Ph.D. Students: NA Human Ethical Approval: IEC/2020/25

Background: To combat the unprecedented spread of SARS-CoV-2 infection, several vaccines were rapidly developed and made available for human use. The wild-type virus/sequence was used for the development of these vaccines. Given the explosive third wave and observed sequence variations in the spike protein, evaluating the immunogenicity of these vaccines against the Omicron variant was of utmost importance. The need for the development of appropriate neutralization tests was urgent and obvious.

Objectives: To standardize SARS-CoV-2 Omicron-subvariant-specific PRNTs and/or micro-PRNT

Work done: Following Omicron subvariants were used to standardize (1) PRNT (24-wells) and micro-PRNT (96-well format).

1. BA.5 (CD/22/0816)
2. Xbb 1.16 (CD/23/2011)

For both variants, plaque assay was initially optimized in both formats. The optimized parameters were different for the two formats. The optimized parameters were further used to standardize the corresponding neutralization tests. Employing these tests the efficiency

of vaccine/natural infection-induced antibodies in neutralizing Omicron subvariants was determined compared to the wild-type virus. As testing against the Xbb variant was required by the vaccine industries, the tests were validated as per ICH (Q2) guidelines.

Conclusion: BA.5 SARS-CoV-2 variant specific PRNT50 test was developed and Xbb1.16 SARS-CoV-2 variant specific PRNT50 test was developed and validated.

11. Title: To study the effect of microRNA on Chikungunya Virus (CHIKV) replication. (Project ID: CD/23/8/I) Funding: Intramural Duration: April 2023 – Mar 2024 Sanctioned Amount: NA Investigators: PI - Dr. Rajashree Patil Ph.D. Students: Pranita Surjuse Human Ethical Approval: NA

Background: The significant conservation of miRNA binding sites between CHIKV genotypes and closely related RNA viruses suggests an important role in the virus life cycle. As the sites are retained within viral genomes throughout the evolution, they might provide a replicative advantage to the virus. If the sites were deleterious for the virus, selective pressure would have been removed from the viral genome during the evolution. Hence, we hypothesize that these highly conserved putative miRNA binding sites might play an important role in CHIKV replication.

Objectives:

1. To study the effect of miR-214 on CHIKV replication.
2. To understand the interaction between PCBP2 and CHIKV RNA

Work done: The whole genome sequences of all CHIKV genotypes (n=615) were aligned using the Virus Pathogen Database and Analysis Resource (ViPR). The putative hsa-miR-214 showed significant conservation on CHIKV genomes according to the multiple sequence alignment. Hence, we aim to study the effect of miR-214 on CHIKV replication. In addition, In-Silico studies indicated that RNA binding protein, Poly-C binding protein-2 (PCBP2), interacts with the CHIKV genome. Hence, we studied the interaction between PCBP2 and CHIKV RNA in in-vitro settings.

To study the effect of miR-214 on CHIKV replication, we first transfected the cells with miR-214 and then HEK MSR cells were infected with CHIKV at 0.1 MOI. Similar procedure followed in miR-214 downregulated HEK MSR cells. We observed that upregulation of miR-214 decreased CHIKV replication and downregulation of miR-214 levels in HEK MSR cells increases CHIKV replication (Figure. 18). miR-214 was found to be antiviral host factor during CHIKV replication. Although increase in CHIKV

replication was marginal after miR-214 downregulation this result needs further validation in stable miRNA expression system.

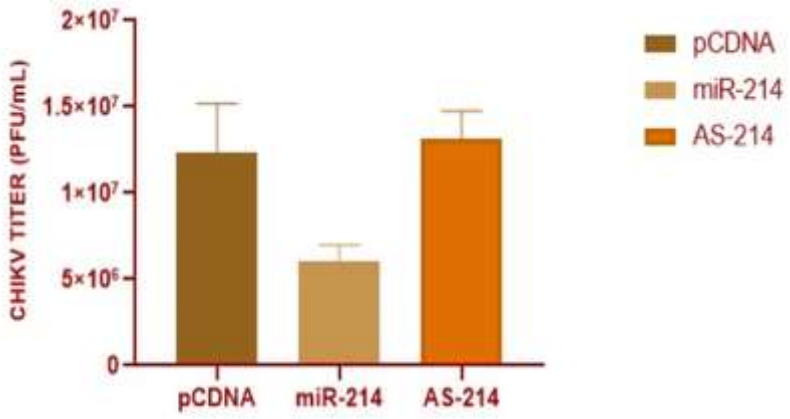

Figure 18. Effect of miR-214 on CHIKV replication. HEK MSR cells were transiently transfected (Lipofectamine 2000) with pcDNA and pcDNA-pri-mir-214(100ng) plasmid and AS-214(100ng) plasmid for upregulation and downregulation of miR-214 respectively. HEK MSR cells transfected with pcDNA (100ng) plasmid, was taken as control. These cells were then infected with CHIKV at 0.1 MOI 24hours post transfection. And plaque assay was performed 48 hours post CHIKV infection to determine the CHIKV titer.

Further, to study effect of PCBP2 on CHIKV replication levels of PCBP2 were modulated with PCBP2 specific siRNA and plasmid expressing PCBP2 in HEK MSR cells. To study effect of PCBP2 overexpression pcDNA-PCBP2 plasmid transfection performed in HEK MSR cells and after 24 hours transiently transfected cells were infected with CHIKV. It was observed that PCBP2 acts as proviral host factor whose upregulation resulted in enhancement in CHIKV replication (Figure. 19a). To validate this effect, further we downregulated PCBP2 levels in HEK MSR cells with PCBP2 gene specific siRNA and then CHIKV infection given to these cells. This resulted in significant decrease in CHIKV replication which confirmed the finding that PCBP2 is proviral host factor which is critical requirement for CHIKV replication (Figure. 19b).

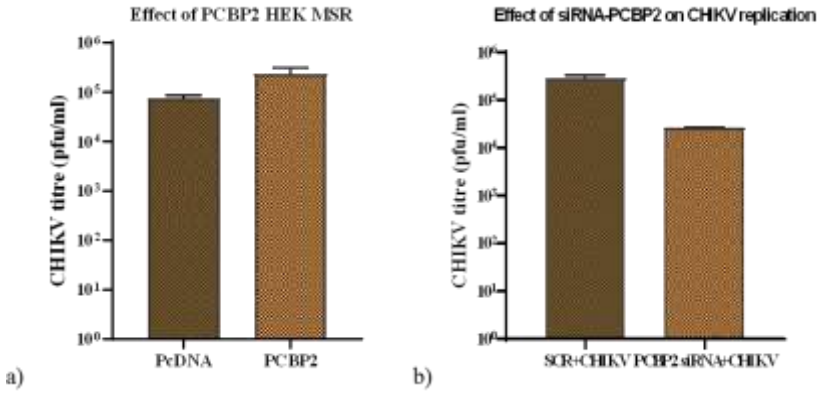

Figure 19. Effect of PCBP2 on CHIKV replication a) HEK MSR cells were transfected with 25 pmoles siRNA-PCBP2 and siRNA scrambled (negative control) b) HEK MSR cells were transiently transfected (Lipofectamine 2000) with pcDNA (500ng) as control and pcDNA-PCBP2 (500ng), with Lipofectamine 2000. 24 hours post transfection same cells were infected with 0.001 MOI CHIKV and harvested 48 hours post infection. Plaque assay was performed to determine the CHIKV titer.

Now that we know the effect of miR-214 is antiviral and PCBP2 is proviral we wanted to find out what is combined effect of both of these host factors on CHIKV replication. Here we have used stable miR-214 overexpressing and sequestered HEK MSR cells. This stable system was chosen to keep one of the parameter constant and reduce variability in results. If PCBP2 and miR-214 both were transiently expressed then actual effect of any host factor could not be understood. These stable cells were transfected with pcDNA-PCBP2 plasmid. It was observed that miR-214 overexpression did not allow PCBP2 to show its proviral role. Although PCBP2 levels were maintained high, still miR-214 decreases CHIKV replication. On the other side miR-214 sequestration lead to enhancement of CHIKV replication where PCBP2 effect was visible (Figure. 20). Here miR-214 might show some regulatory effect on PCBP2 during CHIKV replication. To identify these regulatory effect further experiments are required.

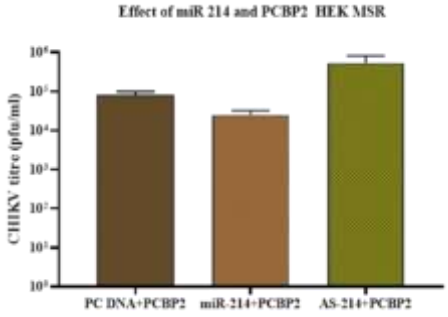

Figure 20. Effect of miR-214 and PCBP2 on CHIKV replication. HEK MSR Stably expressing pcDNA, pcDNA-pri-mir-214, AS-214 were transfected with PCBP2 (500ng) by Lipofectamine 2000. These cells were then infected with CHIKV at 0.001 MOI, and the virus titre was calculated by plaque assay.

Conclusion: Our data suggests that miR-214 exhibits antiviral role on CHIKV replication and PCBP2 acts as a proviral factor for CHIKV replication.

12.Title: Seroprevalence of anti-hepatitis A virus antibodies in four cities from different parts of India. (Project ID: CD/23/1/E) Funding: Extramural (GSK) Duration: 2021 to 2024 Sanctioned Amount: 20 Lakhs Investigators: PI – Dr. S Lalwani (Bharati Vidyapeeth Medical College & Hospital), Dr Vidya A. Arankalle (IRSHA); Collaborators: Dr. Sonali Palkar (Bharati Vidyapeeth Medical College & Hospital, Pune); Dr. Monjiri Mitra (Institute of Child Health, Kolkata); Dr. Balasubramanian S (Kanchi Kamakoti CHILDS Trust Hospital, Chennai); Dr. Gurmeet Kaur (Christian Medical College & Hospital, Ludhiana). Ph.D Students: NA Human Ethical Approval: IEC/2019/66

Background: Hepatitis A, mainly caused by contaminated water and food, was earlier thought to be restricted to children in resource-restricted nations. However, as the prevalence of hepatitis A is inversely proportional to socioeconomic status, India has been experiencing a definite change in hepatitis A virus (HAV) epidemiology. Pune, western India was earlier identified as hyperendemic for hepatitis A. Subsequently, we noted age- and socioeconomic status-dependent reduction in hepatitis A virus (HAV) prevalence.

Objectives:

1. To assess age-stratified anti-HAV positivity in different parts of India as represented by four metropolitan cities in the northern/southern/eastern/western regions.
2. To classify different populations based on the WHO criteria for HAV endemicity:
3. To understand overall and region-wise risk factors associated with anti-HAV positivity

Work done: Institutional Ethics Committee of Bharati Vidyapeeth (Deemed to be University), Pune, (DCGI Reg. No. ECR 313/Inst/MH/2013/RR-19) approved this study vide letter IEC/2019/66, dated 23rd September 2019.

As per age group-anti-HAV-positivity-specific sample size calculations (1-40 years), 496 samples/site were collected from Pune, Kolkata, Chennai, and Ludhiana. All the samples were tested for anti-HAV antibodies using ELISA.

Anti-HAV positivity:

Figure 21 depicts age-stratified anti-HAV antibody positivity in the four cities included in this study. Overall, 44.9% of children up to the age of five years were anti-HAV positive,

with anti-HAV seropositivity increasing with increasing age group, reaching 92.9% positivity among the 26–40-year-old age group. Thus, 34.6% (199/575) of the population by the age of 15 years, and 18.5% (31/168) of the population by the age of 25 years were anti-HAV negative, and hence susceptible to HAV. The city-wise analysis documented that though the overall pattern was similar, a few differences were evident. In the youngest age group, the lowest seropositivity was seen in Pune (26.8%), whereas 65.2% of the children evaluated in Chennai were already exposed to HAV ($p<0.0001$). Compared to 1-5 years, antibody positivity in the 6-10 age group was reduced in Chennai and Kolkata. However, the differences were not significant ($p=0.15$ and 0.18 respectively). The seropositivity in Kolkata was lowest in the 16-25 age group, lower than in Pune and Chennai ($p<0.001$ for both). Though statistically insignificant ($p=0.09$), lower anti-HAV positivity was seen in Kolkata (61.9%) and Ludhiana (78.6%). The exposure in the 26-40 years age group was comparable in all the cities ($p>0.05$).

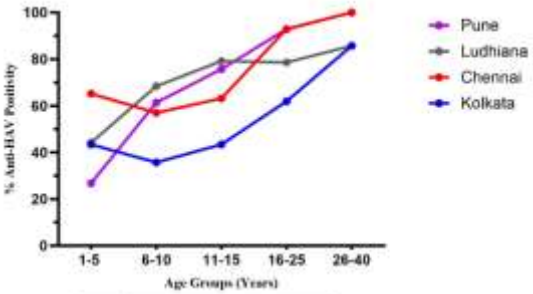

Figure 21. Age-stratified anti-HAV antibody seroprevalence in four metropolitan cities of India

Classification of HAV endemicity:

Classification of HAV endemicity has been proposed by the WHO based on seroprevalence rates. Application of this criteria classified Pune, Chennai, and Ludhiana in the intermediate endemicity zone, while Kolkata was in low HAV endemicity. When all the cities were considered together, metropolitan India could be classified as “intermediate endemicity”, a sign of improved social and personal hygiene.

Risk factors associated with HAV exposure:

When the overall population was considered, multivariate analysis identified age and the use of public toilet facilities as the independent variables associated with higher anti-HAV positivity. Given the regional differences in anti-HAV positivity patterns, city-wise risk factor analysis was carried out. None of the cities exhibited any association of anti-HAV positivity with a history of (H/O) jaundice, family size, and washing hands before eating or after defecation. Age was the only independent risk factor common to all four cities. We did identify city-specific risk factors associated with higher HAV exposure. These included socioeconomic status for Pune, drinking water source and treatment for Chennai, socioeconomic status, and drinking water source for Ludhiana, and use of public toilet facility for Kolkata. Taken together, transmission of HAV was differentially influenced in different regions.

Conclusion: The lowering of anti-HAV positivity reflects a definite improvement in sanitation and voluntary vaccination. Additionally, well-defined efforts are necessary to reduce epidemics of hepatitis A and infections among adolescents/adults that lead to severity and hospitalizations.

13.Title: Age-stratified IgG-anti-Measles virus antibody seroprevalence from four metropolitan Indian cities from different parts of India. (Project ID: CD/23/9/I) Funding: Intramural Duration: Apr 2023 – Mar 2024 Sanctioned Amount: NA Investigators: PI – Dr Vidya A. Arankalle; Co-investigator – Dr. Shubham Shrivastava; Collaborators – Dr. Sanjay Lalwani, Dr. Sonali Palkar (Bharati Vidyapeeth Medical College & Hospital, Pune); Dr. Monjiri Mitra (Institute of Child Health, Kolkata); Dr. Balasubramanian S (Kanchi Kamakoti CHILDS Trust Hospital, Chennai); Dr. Gurmeet Kaur (Christian Medical College & Hospital, Ludhiana). Ph.D Students: NA Human Ethical Approval: IEC/2019/66

Background: Measles is a highly contagious disease that can lead to several complications and death. A safe and effective vaccine is available. To provide herd immunity that will lead to eliminating illness, a sustained vaccination coverage of 95% is necessary [1]. Following the WHO initiative of achieving measles and rubella elimination by 2023, India aims for vaccination coverage of 95% with two doses of MR vaccine. A cross-sectional study conducted at Pune during 2016-17 employing 150 samples/group collected at 6/9 months (no immunization) and 12/15 months (at least 4 weeks post-vaccination) showed that >25% of vaccinated children were negative for IgG-anti-measles virus (IgG-anti-MV) antibodies. The low seroconversion rate among children with a definite immunization history was of concern.

Objective: To assess anti-measles antibody positivity among children from four metropolitan cities aged 1-5 years.

Work done: To understand if a low anti-measles antibody response rate is an isolated observation, we tested serum samples collected from 2020 to 2022 for HAV prevalence. The Institutional Human Ethics Committee approved the study. Based on the 74.4% IgG-anti-MV antibody prevalence at 18 months of age and expected persistence till 5 years, the sample size of 296 was calculated. However, being a retrospective analysis, we tested 529 serum samples from children aged 1-5 years from four metropolitan cities situated in the western (Pune), eastern (Kolkata), southern (Chennai), and northern (Ludhiana) parts of India. The sample collection was delayed when lockdown was imposed but continued at other times. A subset of IgG-anti-MV positive samples was screened for IgM-anti-measles antibodies. The history of measles immunization was not available.

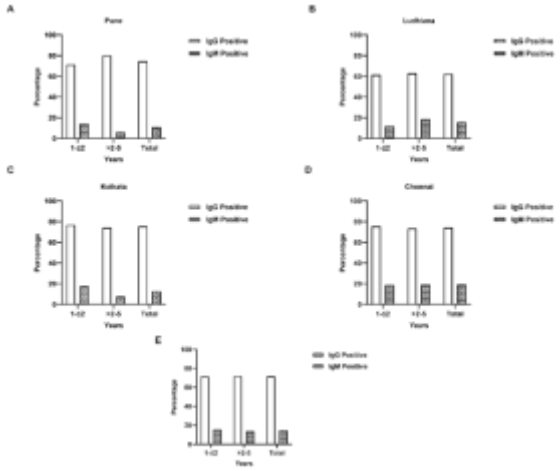

Figure 22. Percentage seropositivity of IgG and IgM-anti-Measles Virus (MV) antibodies in children of 1 to ≤ 2 and >2 to 5 years age groups in (A) Pune, (B) Ludhiana, (C) Kolkata, (D) Chennai and (E) combined-India.

Surprisingly, the IgG-anti-MV antibody positivity was low across all four cities (Figure 22). Overall seropositivity of 75% (74.1-75.4%) was recorded in Pune, Chennai and Kolkata. In Ludhiana, though statistically insignificant, only 62.3% of children were IgG-anti-MV positive. IgM positivity indicative of recent infection was seen in 10.7-19.1% of the IgG positives tested. At the time of sample collection, measles-like symptoms were not seen and probably reflected asymptomatic / breakthrough infections, though subsequent follow-up was not undertaken. The strikingly low antibody positivity remains a matter of concern.

Conclusion: Our results emphasize the need for immunogenicity analysis in a subset of samples to ensure the desired outcome of >95% measles vaccine coverage for which the government of India is implementing targeted efforts.

Other Information

Budget

Extramural Grants (newly sanctioned and ongoing) Total Projects: 41; Funds Recd: Rs.1179.71 Lakhs

Budget							
S. No	Name of the Scheme/Project/ Endowments/ Chairs	Name of the Funding agency	Year of Award	Funds provided (INR in lakhs)	Duration of the project	Funds Reced in April 2023-March 2024	Revenue generated (INR in Lakhs) as per AQAR
1	Capacity enhancement of National Immunogenicity and Biologics Evaluation Center for assessing the immunogenicity of SARS-CoV-2 vaccines	DBT-BIRAC	2021	134.15	Feb 2021-Feb 2023	134.13	
2	Establishment of National Centre for Immunogenicity Testing, NCIT to evaluate vaccines in clinical trials	DBT-BIRAC	2019	160.00	2019-2023	63.54	
3	Development of potent adjuvanted respiratory syncytial virus vaccine for mucosal delivery	Wellcome-DBT Indian Alliance	2019	168.93	2019-2023	52.85	
4	Repurposing of cephalosporins in cervical cancer treatment.	EMR-ICMR	8 Sep 2021	31.15	2021-2024	Nil	
5	Phytochemical standardization and evaluation of anti-cancer and immunomodulatory activity of Unani formulation, Itrifal Gudadi.	Expression of Interest Scheme, CCRUM	11 March 2020	43.57	2020-2023	9.88	

6	Continued Medical Education Program (CME) on Effective Science Communication for Ayush teachers	Rashtriya Ayurveda Vidyapeeth (RAV), Ministry of Ayush		9.00		Nil	
7	Evaluation of Phonophoresis Therapy with Myostaal Gel in participants suffering from Acute Musculoskeletal Conditions: A Randomised, Controlled Clinical Study	Solumiks Herbaceuticals Pvt. Ltd.	Aug 2022	4.80	2022-2023	1.18	
8	Effect of Lipitaezar tablets, a proprietary formulation in patients suffering from Non-alcoholic fatty liver disease (NAFLD): an open label, randomized, controlled clinical study	Amardeep Pharma Pvt. Ltd.	August 2023	5.41	2023-2024	4.32	
9	A comparative efficacy study of Nishamalaki and Metformin in lean and obese females suffering from Polycystic Ovary syndrome (PCOS) along with focus on fatty acid composition	Shree Dhootpapeshwar Ltd.	May 2024	4.35	May 2024-onwards	1.74	
10	Effect of Madhavbaug Treatment Regimen on Oxidative Stress and Inflammation in Cardiovascular Disease (CVD)	Madhavbaug (Vaidya Sane Ayurved Laboratories Ltd.)	2023		2023-2024	4.24	

11	Identification of Nadi patterns in individuals with different glycemic profiles using AI based technology and their validation for mass screening of T2DM' with Atreya Innovations Pvt. Ltd.	Attreya Innovations Pvt. Ltd. – Dr. Supriya	January 2024	6.03	January 2024-ongoing	2.41	
12	ICAR –AICRP-Linseed Value Addition Centre	ICAR	2015	17.77	2015 onwards	29.98	
13	Extraction of bioactive lignan and development of value added products from flaxseed	SERB-IRRD	2019	27.85	2022	Nil	
14	Polyunsaturated fatty acid enriched nano-formulation for diabetes: In vivo efficacy and bioavailability studies	Chellaram Diabetes Research Centre	2022	27.38	2022-2025	10.55	
15	Investigating Mechanisms Leading to Preeclampsia	Indian Council of Medical Research, Centre for Advanced Research	2017	757.95	2017-2022	Nil	
16	Exploring the effect of prenatal omega-3 fatty acid supplementation on cognitive performance in the offspring born to dams with gestational diabetes mellitus	Dr. Nisha Kemse ICMR DHR	2021	46.6	2021-2023	Nil	
17	Evaluation of different adjuvants for development of potent chikungunya vaccine	DST SERB Dr. Harshad Patil	2018	32.2	May 2018 – May 2021	2.01	
18	Seroprevalence of anti-hepatitis A antibodies in four cities from different parts of India	GSK –HAV	2019	20.00	2019-2022	1.97	

19	Exploring the role of maternal fatty acids, placental fatty acid metabolism, and inflammation in determining infant health in gestational diabetes mellitus	DBT GDM	2022	95.18	2022-2025	48.65	
20	Early Interventions to Support Trajectories for Healthy Life in India (EINSTEIN). Healthy Life Trajectories Initiative (HeLTI)	DBT HELTI	Dec 2017	Total Sanctioned Rs. 743.44 Lakhs; IRSHA Share: Rs.13.50 Lakhs	2017-2025	3.70	
21	Epigenetic regulation of placental peroxisome proliferator activated receptor (PPAR) in women delivering low birth weight babies	DBT Biocare – Dr. Deepali Sundrani	July 2019	35.50	2019-2022	4.42	
22	Understanding the association and underlying molecular mechanisms of early life 'Double-burden' of malnutrition and non-communicable disease risk in adolescence	DBT Adolescent Project	Oct 2023	158.95	2023 to 2026	53.93	
23	Building evidence and designing solutions to prevent stillbirths in India – a collaborative approach to retrospectively analyze pregnancy cohorts in India	ICMR Still Birth Project	Feb 2024	8.06	Feb 2024-Aug 2024	8.06	
24	Platelet derived exosomes and their role in endothelial dysfunction in dengue infection	DBT Biocare – Dr. Shubham	March 2019	46.4	March 2019 – March 2022	5.10	
25	A Phase I single blind randomized placebo	Abiogenesis Clinpharm	2023	NA	2023-2024	129.75	188.29

	controlled study to evaluate the safety and immunogenicity of live attenuated tetravalent recombinant dengue vaccine of HBI in healthy adults of 18 to 50 years of age (Stage 1)	Dr. Shubham / Dr. Deepali Mali					
26	Prospective, multi-center, randomized, open label, active control, phase 2 clinical study to evaluate immunogenicity, safety and tolerability of single heterologous booster dose of RelCoVax (Protein Subunit Vaccine of Reliance Life Sciences against SARS-CoV-2 Virus) with Corbevax (Protein Subunit Vaccine of Biological E Ltd. against SARS-CoV-2 Virus)	Reliance – Dr. Ruta	2023	NA	2023-2024	32.15	27.75
27	Anti-Viral Efficacy Evaluation against SARS-CoV-2 coronavirus (wild variant), Task order 18	ITC Ltd. – Dr. Rashmi	2023	NA	2023-2024		1.08
28	Immunogenicity study of an mRNA vaccine candidate HGCO-19 against SARS-CoV-2(Stage 1)	Gennova Biopharma – Dr. Ruta	2021	NA	2021-2024	83.01	4.96
29	A Phase II, Single blind, Randomized, Parallel group, Dose ranging, Single Dose Study of Dengue Monoclonal antibody (Dengue mAb) in Adults with Dengue Fever	Serum Institute of India – Dr. Ruta	2023	NA	2023-2026	60.00	60
30	A Seamless Phase II/III, Observer-blind,	Bharat Biotech	2023	NA	2023-2026	144.92	144.92

	Multi-Centre, Randomized Clinical Trial to Evaluate Immunogenicity and Safety of BBV87, an Inactivated Chikungunya Virus Vaccine in Healthy Subjects 12-65 Years of Age (Stage 2)	Internationa l Ltd. – Dr. Shubham					
31	Immunogenicity study of an mRNA vaccine candidate HGCO-19 against SARS-CoV-2(Stage 1)	Gennova Biopharmac euticals Ltd. –Dr. Ruta	2021	NA	2021-2022	46.66	83.01
32	A prospective, open-label, single arm, multicenter, phase III clinical study to evaluate the immunogenicity and safety of 3mg (2 dose) regimen of Novel Corona Virus -2019-nCov vaccine candidate of M/s Cadila Healthcare Limited by intradermal route in healthy subjects	Zydus Lifesciences Ltd.- Dr. Ruta	2023	NA	2023-2024	136.75	54.06
33	Anti-Viral Testing of NCEs	Sai Lifesciences Ltd. –Dr. Sudha/ Dr. Rashmi	2022	NA	2022-2023		7.93
34	A phase 2, observer-blind, randomized study to assess the safety and immunogenicity of heterologous prime-boost COVID-19 vaccines regimens in individuals aged 18 to 65 years in Mozambique and Madagascar	Internationa l Vaccine Institute Korea- Dr. Shubham	2023	NA		55.11	55.09

35	Establish serial Sero-Surveillance to monitor the trend of SARS-CoV-2, Dengue and Chikungunya infection transmission in general population India (KEM site/Share India)	KEM Hospital & Research Centre/ Share India- Dr. Rashmi	2023	NA	2023-2026	35.64	35.81
36	ISO 21702 and ISO 18184	Anabio Technology –Dr. Rashmi	2022	NA	2022-2023		3.16
37	Antiviral efficacy of drug against SARS-CoV-2 virus	Torrent Pharma. Ltd. –Dr. Rashmi	2023	NA	2023-2024	2.36	2.36
38	Evaluation of Recoverz Capsules against SARS-CoV 2 Wild Strain	Opus Die Foundation –Dr. Rashmi (not my project)	2021	NA	2021-2022		2.36
39	Services for Dengue PRNT (Training and material transfer)	Drugs for Neglected Diseases – Dr. Shubham Shrivastava	2023	NA	2023-2024	10.70	10.7
40	Establish serial Sero-Surveillance to monitor the trend of SARS-CoV-2, Dengue and Chikungunya infection transmission in general population India (KEM site/Share India)	Share India –Dr. Rashmi	2023	NA	2023-2026		28.89
41	Generation of Neutralizing Antibodies to Dengue Virus	Reliance – Dr. Ruta	2023	NA	2023-2024		0.85
	Total					**1179.71**	

Intramural funding:

Sr. No	**Name of the Project**	**Funding Agency**	**Sanctioned (INR)**	**Received (INR)**	**Expenditure (INR)**

1	Investigating effect of Triphala in patients suffering from Non-alcoholic fatty liver disease (NAFLD): a proof of concept clinical study	Bharati Vidyapeeth Deemed University – Dr. Poonam Gupte	1,00,000/-	1.00	0.16
2	In vivo efficacy studies of novel phytoformulations of selected phytoactives in model of high fat diet induced fatty liver	Bharati Vidyapeeth Deemed University- Dr. Supriya Bhalerao	1,00,000/-	1.00	0.34
3	Comparitive validation of selected wild vegetables for their neutraceutical potential occurs in Western ghats of Maharashtra	Bharati Vidyapeeth Deemed University- Dr. Suresh Jagtap	90,000/-	0.90	0.89
4	Evaluation of heavy metal accumulation in selected medicinal plants	Bharati Vidyapeeth Deemed University- Dr. Anuradha Mulik	90,000/-	0.90	0.72
					2.11

Student Fellowship

S.No	**Funding Agency**	**Tilte of the project**	**Total grant sanctioned (In Lakhs)**	**Amount Received (INR) In Lakhs**
1	Akanksha Mahajan	Evaluation of anticancer potential of selected phytochemicals against breast cancer stem cells	24.56	1.97
2	Rama Rajadnya	Evaluating the effect of selected bioactive on cytokine and chemokine regulation in prostate cancer	23.06	0.20
3	Prajkta Patil	Evaluating the effect of lignans inregulation of lipid and cholesterol metabolism in Breast Cancer	23.06	9.51

4	Samradni Pingale	Phytochemical standardization and evaluation of anti-cancer and immunomodulatory activity of Unani formulation, Itrifal Gudadi.	43.57	Nil
5	Rushabh Waghmode	Repurposing of cephalosporins in cervical cancer treatment.	31.15	Nil
6	Manoj Khawate	Chemometric analysis and development of methodology for quality standardization of Vidanga	5.20	Nil
7	Apoorva Jadhav	Development of a novel symbiotic using *Dioscorea* as a prebiotic against Ulcerative Coilits	5.20	Nil
8	Ms. Nikita Joshi	Placental fatty acid metabolites, oxidation and transport in Gestational Diabetes Mellitus		6.69
	Total			**19.09**

Publications (Total No: 28)

1. Eitisha Sandecha, Dipesh Chikane, Suresh Jagtap, Arvind Kadus and Neelambika Meti. In vitro seed germination of Decalepis hamiltonii an endangered medicinal plant using gibberellic acid and coconut water. Ecology, Environment and Conservation. June-2024
2. Pratiksha Chavan, Trupti Danane, Archana Sharbidre, Sharad Pawar, Apurva Jadhav, Suresh Jagtap. Diosgenin Mitigates Aluminum Chloride Mediated Developmental Toxicity in Drosophila melanogaster June-2024 Toxicology International
3. Sagar Shinde, Jagtap Suresh, Deokule Subhash, Mungikar Rahul and Athoiba Singh Angiosperms, Fabaceae, Mucuna championii Benth. New record to India. Ecology, Environment and Conservation Dec-2023
4. Apurva Jadhav, Suresh Jagtap, Suresh Vyavahare, Archana Sharbidre and Bipinraj Kunchiraman Reviewing the Potential of Probiotics, Prebiotics and Synbiotics: Advancements in Treatment of Ulcerative Colitis Frontiers in Cellular and Infection Microbiology Dec-2023
5. Sourav Mukherjee, Ninad Nangare and Suresh Jagtap Use of Orchids in Ayurveda: Is Substitution Scientific and Appropriate? Journal of Natural Remedies Oct- 2023
6. Bhapkar, V., Giramkar, S., & Bhalerao, S. (2024). Differences in Perception of Body Image among Young and Older Adult Women from Pune City, Maharashtra: A Cross-Sectional Study. Journal of Ayurveda, 18(1), 28-36. doi: 10.4103/joa.joa_253_22
7. Bhalerao, S. S., Joshi, A. A., Khadke, S., & Sathiyanarayan, A. (2024). Anti-obesity Effects of Triphala at Biochemical and Molecular Level in High-Fat Diet-induced Obese

Rats. Pharmacognosy Magazine, 20(1), 30-42. doi: https://doi.org/10.1177/0973129623119831

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12. Khadke, S., Gupte, P., Mourya, A., Yadav, A., Mane, S., Joshi, A., et al. (2023). Immunomodulatory effect of a proprietary polyherbal formulation on healthy participants: A single-blind, randomized, placebo-controlled, exploratory clinical study. Perspectives in Clinical Research. 14(3), 130-138. doi: 10.4103/picr.picr_100_22.
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Book:

Bodhankar S, Hegde MV, Joshi AA, Zanwar AA. Jeevandayinee Jawas (December-2023). Goldenpage Publications, Pune, India. ISBN: 978-81-965069-4-0Book chapters (Total No: 2)

Book Chapter

1. Manimurugan, C., Zanwar, A., Sujatha, M. Genetic Enhancement of Nutraceuticals in Linseed: Breeding and Molecular Strategies. In: Kole, C. (eds) Compendium of Crop Genome Designing for Nutraceuticals. Springer Nature Singapore. https://doi.org/10.1007/978-981-19-3627-2_19-1 2023, Chapter no. 11; 519-543. eBook ISBN: 978-981-19-3627-2

2. Mathangi DC, Bhalerao SS. "Potential role of traditional medicine in stem cell research." In Stem Cells and Signaling Pathways edited by Pathak S, Banerjee A. Academic Press, 2024, pp 451-460.

3. Bhalerao S, Chitrakar M. "Basic Concepts of Therapeutic Nutrition in Ayurveda" In Therapeutic Nutrition in Ayurveda edited by Wanjarkhedkar P, Pathak Y. CRC Press, 2024, pp 1-19.

Patents:

Patent Title	**Name of Innovators**	**Patent Application No.**	**Filling date**	**Current status**
Developement of new herbal ointment for the management of dermatophytic infections	Dr. Suresh Jagtap, Mr. Suraj Bhongale	L-147653/2024	03-05-2024	Registered Copy-right
To develope a new cultivation technique by bioelicitation for Asparagus racemosus wild	Dr. Suresh Jagtap, Mr. Suraj Bhongale	L-148180/2024	09-04-2024	Registered Copy-right

Artificial intelligence associated ultrasonic extraction of Flavonoids	Dr. Varsha Umesh Ghate, Dr. Suresh Jagtap	6357474	06-04-2024	Registered Patent
Artificial intelligence associated ultrasonic extraction of Flavonoids	Dr. Varsha Umesh Ghate, Dr. Suresh Jagtap	413495-001	14-04-2024	Registered Copy-right
Device for Thin Layer Chromatography (TLC)	Dr. Suresh Jagtap	6370145	05-06-2024	Registered Patent
Formulation of edible oil	Zanwar AA, Hegde MV	Indian Patent Application No. 201921006187	16/02/2019	Published on:21/08/2020 Granted on: 30/01/2024 Patent no. 504676
Fatty acids and Δ6 desaturase index threshold as indicators of preeclampsia and method of detection	Dr. Sadhana Joshi	Patent Application No.- 202221071133	Filling date-03/05/2024	Current status: Published
Prediction model for early onset of preeclampsia	Dr. Sadhana Joshi	Patent Application No.- 202321036855	Filling date-03/05/2024	Current status: Published

Awards and Honors:

Faculty				
Sr. No	**Academic Year**	**Name of the Faculty Member**	**Name of Award / Honor**	**Details of Award / Honor**
1	23-24	Dr. Suresh Jagtap	Green ThinkerZ International Award for Outstanding Researchers 2024-reg	International Award for Outstanding Researchers 2024 instituted by the Green ThinkerZ, India which is a registered society under Societies Registration Act (XXI of 1860), Govt of Punjab, India and registered at NGO Darpan, NITI Aayog, Government of India (PB/2022/0310139); advocating United Nation's Sustainable Development Goals 2030: The global Goals and Academic & Research Programs for API and Career Advancement Scheme
2	2023-24	Dr. Supriya Bhalerao	Invited faculty for a Workshop by World Health Organization, Southeast region,	Invited Resource person for workshop on Clinical research methodology in Traditional medicine for WHO Southeast region, Member state- Bhutan
3	2023-24	Dr. Supriya Bhalerao	Invited member for a National Consultative Meet organized by CCRAS, Ministry of Ayush and NIIMH, Hyderabad (WHO collaborating centre for Traditional Medicine	Invited member for National Consultative Meet on Research Priority Settings in Traditional Medicine
4	2023-24	Dr. Anand Zanwar	Best oilseed Centre in Linseed	Indian Council of Agriculture Research (ICAR)

5	2023-2024	Ahmedali Mandviwala	Travel Award	8th RESVINET Conference - A Global Conference on Novel RSV Preventive and Therapeutic Interventions, Mumbai (India), 13-16 February 2024
6	2023-2024	Dr. Harshad Patil	LMIC-ISV Award	International Society of Vaccine Annual Congress, Lausanne, Switzerland, 22-24 October 2023
7	2023	Dr Sadhana Ramchandra Joshi	ICMR- Collaborating Centre of Excellence - (ICMR-CCoE) in recognition of the commendable achievements in biomedical research- Sanction date: 18th September 2023	
Students				
1	23-24	Eitisha Sandecha	Best presentation award	Best presentation award on the theme 'Medical Biotechnology', organized in International conference on 'Innovations in Biotechnology Research for Sustainable Development: Challenge and Practices' Held on 28th and 29th, March 2023 in Association with Microbiologist Society, India.
2	23-24	Apurva Jadhav	Ist Prize for Best Oral Presentation award	Ist Prize for Best Oral Presentation award on the theme 'Fermented foods, Health Status and Social well-being' held on 21st-22nd November 2023 organised by North Eastern Hill University (NEHU)

				Shillong, Meghalaya in Association with SASNET-FF
3	23-24	Ms. Aditi Godhamgaonkar	Best Oral Presentation Award in free communication (clinical nutrition) at 55th Annual conference of NSI held at ICMR-NIN, Hyderabad	25th - 26th November 2023
4	23-24	Dr. Nisha Kemse	Oral Presentation at 55th Annual Conference of the Nutrition Society of India held at the ICMR-National Institute of Nutrition, Hyderabad	25-26 November, 2023

Papers presented in International Conferences/Seminars/Workshops –

Sr. No.	Academic Year	Name of student	Name of Conference	Title of poster/oral presentation
1.	2023-2024	Shweta Chelluboina	6th Edition of World Congress on Infectious Diseases by Magnus Group held on June 24-26, 2024 in Paris, France	Dynamics of Maternal Dengue Virus Antibodies in Indian Infants
2.	2023-2024	Ahmedali Mandviwala	8th RESVINET Conference - A Global Conference on Novel RSV Preventive and Therapeutic Interventions, Mumbai (India), 13-16 February 2024	Dual pattern recognition receptor ligands as adjuvants for prefusogenic F based RSV virus-like particle vaccine candidate
3.	2023-2024	Ms. Aditi Godhamgaonkar	poster presentation at International Federation of Placenta Associations conference held at Rotorua, New Zealand 5th – 8th September 2023,	'Early pregnancy oxidative stress is associated with shorter placental telomeres'

Papers Presented in National Conferences/Seminars/Workshops –

Sr. No.	Academic Year	Name of student	Name of Conference	Title of poster/oral presentation
1.	2023-2024	Sayali Vedpathak	IMMUNOCON 50 - Golden jubilee conference of Indian Immunology Society, from 5th to 8th October 2023, AIIMS, New Delhi	Dengue virus induces alteration of platelet adhesion molecules affecting vascular dysfunction
2.	2023-2024	Shweta Chelluboina	VIROCON 2023 on "Advancements in global virus research towards one health" held during 01–03 December, 2023 at ICAR-National Research Centre for Banana, Tiruchirappalli, Tamil Nadu, India	Development of a microneutralization test for measuring neutralizing and enhancing antibodies against dengue 2 and 4 viruses
3	23-24	Aditi Godhamgaonkar	Oral Presentation in free communication (clinical nutrition) at the 55th Annual conference of NSI held at ICMR-NIN, Hyderabad25th - 26th November 2023	Fatty acids status during pregnancy influences placental telomere length
4	23-24	Dr. Nisha Kemse	25-26 November, 2023 Oral Presentation at 55th Annual Conference of the Nutrition Society of India held at the ICMR-National Institute of Nutrition, Hyderabad, Telangana	"Maternal Omega-3 Fatty Acid Supplementation Improves Brain Neurotrophins and Angiogenic Markers in the offspring Born to Gestational Diabetes Mellitus Mothers
5	23-24	Dr. Kamini Dangat	25-26 November, 2023 Oral Presentation at 55th Annual Conference of the	" Maternal fatty acids status influences fetal

			Nutrition Society of India held at the ICMR-National Institute of Nutrition, Hyderabad, Telangana	biometry: The REVAMP cohort"
6	23-24	Dr. Deepali Sundrani	25-26 November, 2023 Poster Presentation at 55th Annual Conference of the Nutrition Society of India held at the ICMR-National Institute of Nutrition, Hyderabad, Telangana	"Maternal fatty acids influence microRNA regulation of angiogenic factors in Assisted Reproductive Technology (ART) placentae "
7	23-24	Hemlata Pisal	25-26 November, 2023 Poster Presentation at 55th Annual Conference of the Nutrition Society of India held at the ICMR-National Institute of Nutrition, Hyderabad, Telangana	" Physical Activity in Women with Preeclampsia: A Longitudinal Study"
8	23-24	Dr. Juhi Nema	25th - 26th November 2023 Oral Presentation at the 55th Annual conference of NSI held at ICMR-NIN, Hyderabad	"Role of maternal nutrition on angiogenesis in preeclampsia"
9	23-24	Nikita Joshi	25th - 26th November 2023 Oral Presentation at the 55th Annual conference of NSI held at ICMR-NIN, Hyderabad	"Fatty acids and their metabolites (resolvins) are altered in women with gestational diabetes mellitus (GDM)"

Ph. D Degree Awarded: 3

Sr. No	Name of the Student	Name of the Guide	Topic	Month and Year of Award
1	Kinjal Dave	Dr. Sadhana Joshi	Influence of maternal one carbon metabolites on placental epigenetic patterns	July 2023
2	Ms. Aditi Godhamgaonkar	Dr. Sadhana Joshi	Placental telomere attrition in women with preeclampsia	May 2024
3	Ms. Anjali Jadhav	Dr. Sadhana Joshi	Maternal Fatty Acids, Oxidative Stress and Neurotrophins in Gestational Diabetes Mellitus	Dec 2024

Invited Talks by Faculty

Sr. No	Academic Year	Date	Name of the faculty	Topic
1	2023-2024	23/06/2024	Dr. Sadhana Joshi	"Introduction to DOHaD" Invited speaker at the Indian Association of Biological Psychiatry (IABP) National Mid-year Conference, co-organized with the Department of Psychiatry, BVUMC, Pune, on 23rd June 2024.

Collaborations:

National Collaborations:

Sr. No	Name of the Collaborator	Period	Objectives	Status
1	TOXIINDIA	05 Years	Ph.D. Students enrolled and sharing facilities	Ongoing
2	Zoology Department, Savitribai Phule Pune University, Pune	05 Years	Ph.D. Students enrolled and sharing facilities	Ongoing
3	Dr. Girish Tillu, CCIH, University of Pune	2016 till date	Scientific and technical inputs for developing project proposals, Network pharmacology of Ayurvedic formulations	Ongoing

4	Dr. D. C. Mathangi, Professor of Integrative Medicine, Shriramchandra Institute of Higher Education and Research, Porur, Chennai	Feb 2020- till date	Scientific and technical inputs for developing project proposals	Ongoing
5	Dr. Lalita Savardekar, Senior grade Deputy Director, National Institute for Research in Reproductive and Child Health, ICMR, Mumbai	Feb 2020- till date	Scientific and technical inputs for developing project proposals	Ongoing
6	Dr. Upadhyay, President, United World Against Diabetes (NGO)	March 2024 – till date	Screening of individuals in a community setting with respect to metabolic disorders in collaboration	Ongoing
7	IIT, Delhi	2023-2025	Surface Enhanced Raman Spectroscopy (SERS) based detection and quantitation of SARS-CoV-2 and to assess if variants with few amino acid mutations can be differentiated.	Ongoing

Conference/ workshops/ Seminar attended

Type of the Event	Sr. No	Name of the Faculty	Date	Name of the Event	Organized By	Level (International / National / State / Institute)
1.	Training Workshop	Dr. Poonam Gupte	14 – 15 September, 2023	Designing and conduct of clinical trials	ICMR- NITM	National
2.	Symposium	Dr. Supriya Bhalerao, Shital Giramkar	06-08 February, 2024	Accelerating Biology, 2024	C-DAC	National

3.	Workshop	Dr. Supriya Bhalerao, Dr. Poonam Gupte	O9 May, 2024	Good Clinical Practices	IEC, BVDU	Institute
Workshop	01	Dr. Anand Zanwar	September 5-6, 2023	Annual Group Meeting of Linseed	ICAR, New Delhi and Indira Gandhi Agricultural University, Raipur	National

MOU's and Linkages:

Sr. No	**Name of the Partner**	**Objectives**	**Status**
1	TOXIINDIA	Ph.D. Students enrolled and sharing facilities	Ongoing
2	Zoology Department, Savitribai Phule Pune University, Pune	Ph.D. Students enrolled and sharing facilities	Ongoing
3	Dhande Pathlab Diagnostics Pvt. Ltd.	Conduct of tests and provision of test reports	Ongoing
4	Amardeep Pharma LLP	Provision of funding for conduct of projects in collaboration	Ongoing
5	CCRAS, CARI, Bengaluru	Collaborative Research	Ongoing
6	AVN Ayurveda Formulations Pvt. Ltd.	Collaborative Research	Ongoing
7	Atreya Innovations Pvt. Ltd.	Collaborative Research	Ongoing
8	Vaidya Sane Ayurved Laboratories Limited (Madhavbaug)	Collaborative Research	Ongoing
9	Dr. Khadilkar, Hirabai Cowasji Jehangir Medical Research Institute, Pune	Research and developmental projects in the domain of public health to be undertaken in India	Ongoing
10	Shree Dhootpapeshwar Ltd., Mumbai	Provision of funding for conduct of projects in collaboration	Ongoing
11	Dr. Gaurang Baxi, D.Y.Patil College of Physiotherapy, Pimpri, Pune	Research Consultancy and collaboration	Ongoing

12	Chellaram Diabetes Research Centre	Received funding	Ongoing
13	Reliance Life Sciences Pvt. Ltd	Immunogenicity testing for SARS-CoV-2 vaccine trial using SARS-CoV-2 PRNT against wild type and omicron variant	Ongoing
14	INCLEN Trust International, New Delhi	Chikungunya microPRNT testing for AFI surveillance study	Ongoing
15	INCLEN Trust International, New Delhi	Chikungunya microPRNT testing for AFI surveillance study	Ongoing
16	ICMR-National Institute of Epidemiology, Chennai (ICMR-NIE)	Chikungunya microPRNT testing for AFI surveillance study	Ongoing
17	Christian Medical College, Vellore	Chikungunya microPRNT testing for AFI surveillance study	Ongoing
18	Society for Health Allied Research and Education India (SHARE INDIA), Telangana	Chikungunya microPRNT testing for AFI surveillance study	Ongoing
19	ICMR-Regional Medical Research Centre (RMRC), Bhubaneshwar	Chikungunya microPRNT testing for AFI surveillance study	Ongoing
20	Maulana Azad Medical College (MAMC), New Delhi	Chikungunya microPRNT testing for AFI surveillance study	Ongoing
21	Society for Applied Studies, New Delhi	Chikungunya microPRNT testing for AFI surveillance study	Ongoing
22	Pondicherry Institute of Medical Sciences (PIMS), Puducherry	Chikungunya microPRNT testing for AFI surveillance study	Ongoing
23	Andhra Medical College (AMC), Vishakhapatnam Contact: Dr. PJ Srinivas	Chikungunya microPRNT testing for AFI surveillance study	Ongoing
24	Serum Institute of India Private Limited (SIIPL)	Miscellaneous testing services for Serum Institute as per project-specific work order	Ongoing
25	GLAD and Nano CVD lab, Department of Physics, Indian Institute of Technology (GLNC)	Surface Enhanced Raman Spectroscopy (SERS) based detection and quantitation of SARS-CoV-2 and to access if variants with few amino acid mutations can be differentiated.	Ongoing

Other Activities

Sr. No	Type of the Event	Theme	Date	Level (International / National / State / Institute)
1	Health screening camp was arranged at College of Engineering, BVDU	Risk identification for Metabolic disorders	3rd- 4th October, 2023	Institute
2	Health screening camp was arranged at Rajiv Gandhi Institute of IT & Biotechnology, Poona College of Pharmacy, College of Ayurved, BVDU	Risk identification for Diabetes	10th, 11th, 12th January, resp. 2024	Institute
3	Health screening and awareness in collaboration with United World Against Diabetes (NGO) at Atkarwadi, Near Sinhgad fort	Risk identification for Diabetes, Eye check- up and counseling	17th- 18th March, 2024	Institute

Any other activities:

NIBEC participation at Global Bio-India 2023 by Dr. Rashmi Virkar.

Events Organized at IRSHA

Events Organized at IRSHA

- International Yoga Day – The 10th Yoga day was celebrated on 21st June, 2024. A talk by Dr. Leena Phadke, Professor, Department of Physiology, Smt. Kashibai Navale Medical College and General Hospital was arranged and the topic was Neuroscience of Yoga

- National Ayurveda Day- The theme ‘Ayurveda for One Health’, was declared by the Ministry of Ayush, New Delhi. The 9th National Ayurveda Day was celebrated on the 9th of November, 2023. A talk by Dr. Shailesh Deshpande, Head, Education, Chellaram Diabetes Institute was arranged.

- A health screening camp for metabolic disorders was arranged from 27th September – 30th September, 2023

• A health screening camp for assessment of pulse patterns and risk of Diabetes was arranged at Irsha on 15th January, 2024, in commemoration of the Birth Anniversary of the esteemed founder, Honorable Dr. Patangraoji Kadam [Founder - Bharati Vidyapeeth & Founder Chancellor - Bharati Vidyapeeth (Deemed to be University)] and Birthday of Honorable Dr. Vishwajit Kadam [Secretary - Bharati Vidyapeeth & Pro Vice Chancellor - Bharati Vidyapeeth (Deemed to be University)].

Any other activities: Nil

Any other information or relevant photographs about the program which may be included in the report

Any other activities:

NIBEC participation at Global Bio-India 2023 by Dr. Rashmi Virkar.

International Yoga Day- Dr. Leena Phadke, Talk on Neuroscience of Yoga

National Ayurveda Day- Dr. Shailesh Deshpande, Talk on 'Ayurveda for One Health'

Health screening camps

National Ayurveda day celebration, 21st October, 2022 Theme- Ayurveda for Holistic Health

Atkarwadi, Sinhgad

College of Engineering, BVDU

Rajiv Gandhi Institute of IT & Biotechnology

Poona College of Pharmacy - BVDU

College of Ayurved - BVDU

Interactive Research School of Health Affairs - BVDU

Visitors and relevant photographs:

1. Dr. Harshad Patil receiving the LMIC award at International Society of Vaccine Annual Congress, Lausanne, Switzerland

Staff Information

Staff Category	Number
Scientific staff	**19**
Technical Staff	**11**
Ph.D. students	**31**
Administrative	**11**
Project Staff	**51**
Total	**123**

A) Name of the Teaching/ Scientific Staff:

Sr. No.	Name of the Staff	Designation
1	Dr. Akhileshchandra Mishra	Director
2	Dr. Vidya Avinash Arankalle	Senior Scientist
3	Dr. Sadhana Ramchandra Joshi	Professor
4	Dr. Suresh Dnyandeo Jagtap	Associate Professor
5	Dr. Supriya Bhalerao	Associate Professor
6	Dr. Shubham Shrivastav	Associate Professor
7	Dr. Harshad Padmanabh Patil	Associate Professor
8	Dr. Anvita Kale	Assistant Professor
9	Dr. Ruta Kulkarni	Assistant Professor
10	Dr. Deepali Sundrani	Assistant Professor

11	Dr. Rashmi Govind Virkar	Assistant Professor
12	Dr. Kamini Dangat	Assistant Professor
13	Dr. Juhi Nema	Assistant Professor

B) Name of the Technical Staff:

Sr. No.	Name of the Staff	Designation
1	Dr. Poonam Ashish Gupte	Senior Research Assistant
2	Mrs. Hemlata Mahadeo Pisal	Research Assistant
3	Dr. Anuradha Rajendra Mulik	Research Assistant
4	Mr. Kartikey Tanaji Jagtap	Research Assistant
5	Ms. Karuna N. Randhir	Technical Assistant
6	Ms. Vrushali Kadam	Technical Assistant
7	Ms. Shital Ashok Giramkar	Technical Assistant

C) Name of the Administrative Staff:

Sr. No.	Name of the Staff	Designation
1	Mr. Vijaychand Pandurang Gavade	Sub Accountant
2	Mr. Shivaji Dhondiram More	Electrician
3	Mr. Ananda Dinkar Jadhav	Junior Clerk
4	Mr. Nitin Shankar Mote	Junior Clerk
5	Mr. Dilip Kaka More	Trainee Clerk
6	Mrs. Anjali Rajendra Gajare	Junior Clerk
7	Ms. Supriya Anandrao Patil	Laboratory Assistant

8	Mr. Ankush Rambhau Chandere	Driver
9	Mr. Tushar Ashok Shinde	Peon
10	Mr. Vijay Atmaram Dhanwade	Peon

D) Bharati Hospital Staff:

Sr. No.	Name of the Staff	Designation
1	Mrs. Dipali Patole	Clerk

E) Name of the Project Staff & Fellowship Staff:

Sr. No.	Name of the Staff	Designation
1	Ms. Akanksha Mahajan	JRF
2	Ms. Samradni Pingale	JRF-EMR AYUSH UNANI Fellow
3	Mr. AhmedAli Mandviwala	Technician Wellcome DBT
4	Ms. Himanshi Yadav	Project Technician(III)
5	Dr. Nisha Kemse	Women Scientist
6	Mr. Tushar Sarjerao Dalavi	Project Technician
7	Mr. Rushabh Waghmode	RA-ICMR
8	Mr. Manoj M. Khavte	JRF-CSIR
9	Ms. Prajakta D. Patil	JRF-DST Inspire
10	Ms. Sayali Vedpathak	JRF-UGC
11	Ms. Apurva Jadhav	SRF-UGC
12	Ms. Aishwarya Rajan Kharkhanis	JRF-DBT Bio-care
13	Ms. Shweta Madiwale	Project Associate II DBT
14	Ms. Brishty Roy	Project Assistant
15	Ms. Nikita Joshi	SRF

16	Ms. Rama A. Rajadnya	JRF
17	Dr. Revati D. Bhat	Clinical Study Co-Ordinator
18	Ms. Aditi Godhamgaonkar	Project Associate II DBT

F) NCIA Project Staff:

Sr. No.	Name of the Staff	Designation
1	Mrs. Rajashree Patil	Scientist 'B'
2	Ms. Deepali Mali	Scientist 'B'
3	Mr. Muneesh Kumar Barman	Scientist 'B'
4	Ms. Anamika Solaskar	Technical Assistant
5	Mr. ShambhuRaje Sunil Pisal	Technical Assistant
6	Ms. Swati Dnyaneshwar Bargal	Qualitive Assurance Executive
7	Mr. Tushar Lala Bhosale	Technical Officer
8	Mr. Rahul Lalaso Patil	Health Educator
9	Ms. Prajakta Sanjay Rane	Research Assistant
10	Mr. Urmi Majumdar	Research Assistant
11	Ms. Shweta Chelluboina	Research Assistant
12	Ms. Amita Kasana	Research Assistant
13	Mr. Rahul Harishchandra Kadu	Maintenance Engineer
14	Ms. Aabha Thite	Project Assistant
15	Mr. Shubham Kadlag	Junior Research Assistant
16	Ms. Kajal Phadtare	Junior Research Assistant
17	Ms. Sawani Karandikar	Junior Research Assistant
18	Ms. Rajkanya Toge	Junior Research Assistant
19	Ms. Jayshri Bhagat	Junior Research Assistant

20	Ms. Tejashree Shendage	Junior Research Assistant
21	Ms. Anuradha Patil	Junior Research Assistant
22	Ms. Abhilasha Kadu	Junior Research Assistant
23	Mr. Omkar Kalje	Junior Research Assistant
24	Mr. Sourabh Pandharmise	Junior Research Assistant
25	Ms. Shweta Pradip Kulkarni	Junior Research Assistant
26	Mr. Manoj Mohan Kadam	Junior Research Assistant
27	Ms. Komal Pandurang Jadhav	Junior Research Assistant
28	Ms. Meghana Walke	Lab Assistant
29	Mr. Darshan Pravin Kshirsagar	Technician
30	Mrs. Kiran Sameer Shende	Technician
31	Mrs. Prajakta Rishikesh Jaswante	Office Assistant
32	Mr. Amol Kondibhau Ohol	Multitasking Staff
33	Mr. Mahesh Vitthal Humbe	Multitasking Staff

G) Name of the Centre for Innovation in Nutrition Health Disease (CINHD) Staff:

Sr. No.	Name of the Staff	Designation
Scientific Staff		
1	Dr. M. V. Hegade	Director CINHD
2	Dr. P.B. Ghorpade	Emeritus Scientist
3	Dr. Anand Zanwar	Scientist
4	Ms. Asavari Joshi	Scientist
5	Mr. Aniket Mali	Scientist
6	Mr. Rajesh Shyamsundar Kirad	Manager Research & Development

Technical Staff		
1	Mr. Yogesh Badhe	Project Assistant
2	Mr. Pramod Farde	Technical Assistant
3	Ms. Gouri Shinde	Project Assistant
4	Ms. Prajkta Gaikwad	Junior Research Assistant

H) Name of the PhD Student & Fellowship Staff:

S.No	Year of enrollment	Name of the Student	Student enrollment number (PRN)	Date of enrollment	Gender	Program admitted to	Year and Month of Completion
1	2015-16	Ms. Minal Mahajan	1502015	01/09/2015	Female	Ph.D.	Ongoing
2	2015-16	Ms. Shital Giramkar	1502012	01/09/2015	Female	Ph.D.	Ongoing
3	2016-17	Mr. Amol Chaudhary	1716020162	26/05/2017	Male	Ph.D.	Ongoing
4	2017-18	Ms. Mrunal Gosavi	1716020164	02/09/2017	Female	Ph.D.	Nov. 2022
5	2017-18	Ms. Juhi Nema	1716020166	02/09/2017	Female	Ph.D.	Feb. 2023
6	2017-18	Mr. Kartikey Jagtap	1716020157	02/09/2017	Male	Ph.D.	Apr-23
7	2017-18	Mrs. Asavari A. Joshi	1716020163	02/09/2017	Female	Ph.D.	Ongoing
8	2017-18	Ms. Anjali Jadhav	1716020167	02/09/2017	Female	Ph.D.	Ongoing
9	2017-18	Ms. Kinjal Dave	1716020172	02/09/2017	Female	Ph.D.	Ongoing
10	2017-18	Ms. Amrita Ulhe	1716020159	02/09/2017	Female	Ph.D.	Ongoing
11	2017-18	Ms. Apoorva Parimoo	1716020161	02/09/2017	Female	Ph.D.	Ongoing
12	2017-18	Ms. Nidhi Sharma	1716020171	02/09/2017	Female	Ph.D.	Ongoing

13	2017-18	Mr. Manoj khavate	1716020158	13/02/2018	Male	Ph.D.	Ongoing
14	2018-19	Ms. Akansha Mahajan	1916020004	16/10/2018	Female	Ph.D.	Ongoing
15	2018-19	Ms. Rama Rajadnya	1916020002	16/10/2018	Female	Ph.D.	Ongoing
16	2018-19	Mr. Mayur Aswani	1916020003	16/10/2018	Male	Ph.D.	Apr-23
17	2018-19	Ms. Prajakta Biradar	1916020005	17/01/2019	Female	Ph.D.	Ongoing
18	2019-20	Ms. Aditi Godhamgaonkar	1916020163	29/11/2019	Female	Ph.D.	Ongoing
19	2019-20	Ms. Anu C	1916020161	29/11/2019	Female	Ph.D.	Ongoing
20	2019-20	Mr. Suraj Bhongale	1916020165	29/11/2019	Male	Ph.D.	Ongoing
21	2019-20	Ms. Sayali Vedpathak	1916020167	29/11/2019	Female	Ph.D.	Ongoing
22	2019-20	Ms. Shweta Chelluboina	1916020166	29/11/2019	Female	Ph.D.	Ongoing
23	2020-21	Mr. Mandiwala Ahmedali	2116020159	16/03/2021	Male	Ph.D.	Ongoing
24	2020-21	Mr. Shrikant Thopte	2116020164	17/03/2021	Male	Ph.D.	Ongoing
25	2020-21	Mr. Prashant Dange	2116020165	17/03/2021	Male	Ph.D.	Ongoing
26	2020-21	Ms. Madiwale Shweta	2116020167	17/03/2021	Female	Ph.D.	Ongoing
27	2020-21	Ms. Gauri Vasant Ligade	2116020168	17/03/2021	Female	Ph.D.	Ongoing
28	2020-21	Mr. Mahesh Ekbote	2116020172	17/03/2021	Male	Ph.D.	Ongoing
29	2021-22	Ms. Apurva Jadhav	2116020173	30/11/2021	Female	Ph.D.	Ongoing
30	2022-23	Ms. Prajakta Gaikwad	2216020167	21/07/2022	Female	Ph.D.	Ongoing
31	2022-23	Ms. Vallari Nisargand	2216020168	18/08/2022	Female	Ph.D.	Ongoing

Institutional Committees

SCIENTIFIC REVIEW COMMITTEE

Name and Designation	Role
Dr. Akhilesh Chandra Mishra Director IRSHA.	Chairperson
Dr. Sadhana Joshi Professor & Head, Department of Nutritional Medicine, IRSHA.	Member
Dr. Vidya Arankelle Senior Scientist, Head, Department of Infectious Diseases, IRSHA.	Member
Prof. Mahabaleshwar Hegde Scientific Advisor, Centre for Innovation in Nutrition Health Disease, IRSHA.	Member
Dr. Supriya Bhalerao Associate Professor, Department Obesity, IRSHA.	Member Secretary

INSTITUTIONAL BIOSAFETY COMMITTEE (IBSC)

Approved by DBT, India

Name and Designation	Role
Dr. Akhilesh Chandra Mishra Director IRSHA.	Chairman
Dr. Vijay Bondre	DBT nominee
Dr. Harshad Patil Associate Professor, Department of Communicable Disease, IRSHA.	Member Secretary
Dr. Meera Modak	Outside Expert
Dr. Supriya Bhalerao Associate Professor, IRSHA, Bharati Vidyapeeth University, Pune.	Biosafety Officer

Dr. Vidya Arankelle Senior Scientist, IRSHA, Bharati Vidyapeeth University, Pune.	Internal Experts
Dr. Aniket Mali Associate Professor, IRSHA, Bharati Vidyapeeth University, Pune.	
Dr. Deepali Sundrani Assistant Professor, IRSHA, Bharati Vidyapeeth University, Pune.	

PURCHASE REVIEW COMMITTEE

Name and Designation	Role
Dr. Akhilesh Chandra Mishra Director IRSHA.	Chairperson
Dr. Sadhana Joshi Professor & Head, Department of Nutritional Medicine, IRSHA.	Member
Mr. Vijaychand Gavade Sub-Accountant, IRSHA.	Member
Dr. Harshad Patil Associate Professor, Department of Communicable Disease, IRSHA.	Member Secretary