Annual Report

2018-2019

Bharati Vidyapeeth (Deemed to be University)

INTERACTIVE RESEARCH SCHOOL FOR HEALTH AFFAIRS

IRSHA
INTERACTIVE RESEARCH SCHOOL FOR HEALTH AFFAIRS

Bharati Vidyapeeth Deemed University
Interactive Research School for Health Affairs (IRSHA)
Annual Report July 2018- June 19

Overview of Director

It is my privilege to present the Annual report of Interactive Research School for Health Affairs (IRSHA) for the year 2018-19. We at IRSHA have been sanctioned funds worth Rs.16.00 crores from national funding agency for establishing a "National Centre for Immunogenicity Testing, NCIT to evaluate vaccines in clinical trials. All the departments of IRSHA were successful in receiving financial support of Rs.1129.73 Lakhs from national funding agencies for carrying out their research work. This year student fellowships of Rs. 32.36 lakhs were received. In the current year 3 students were awarded PhD degree.

Two of our laboratories were reaccreditated by NABL for testing of fatty acids, estimation of PRNT and ELISA for NS1 and IgM and two new tests Chikungunya PRNT and Influenza HI were included in the scope of NABL

In the year 2018-19 research work at the institute culminated into 18 publications research articles; 1 book chapter and 3 patent applications.

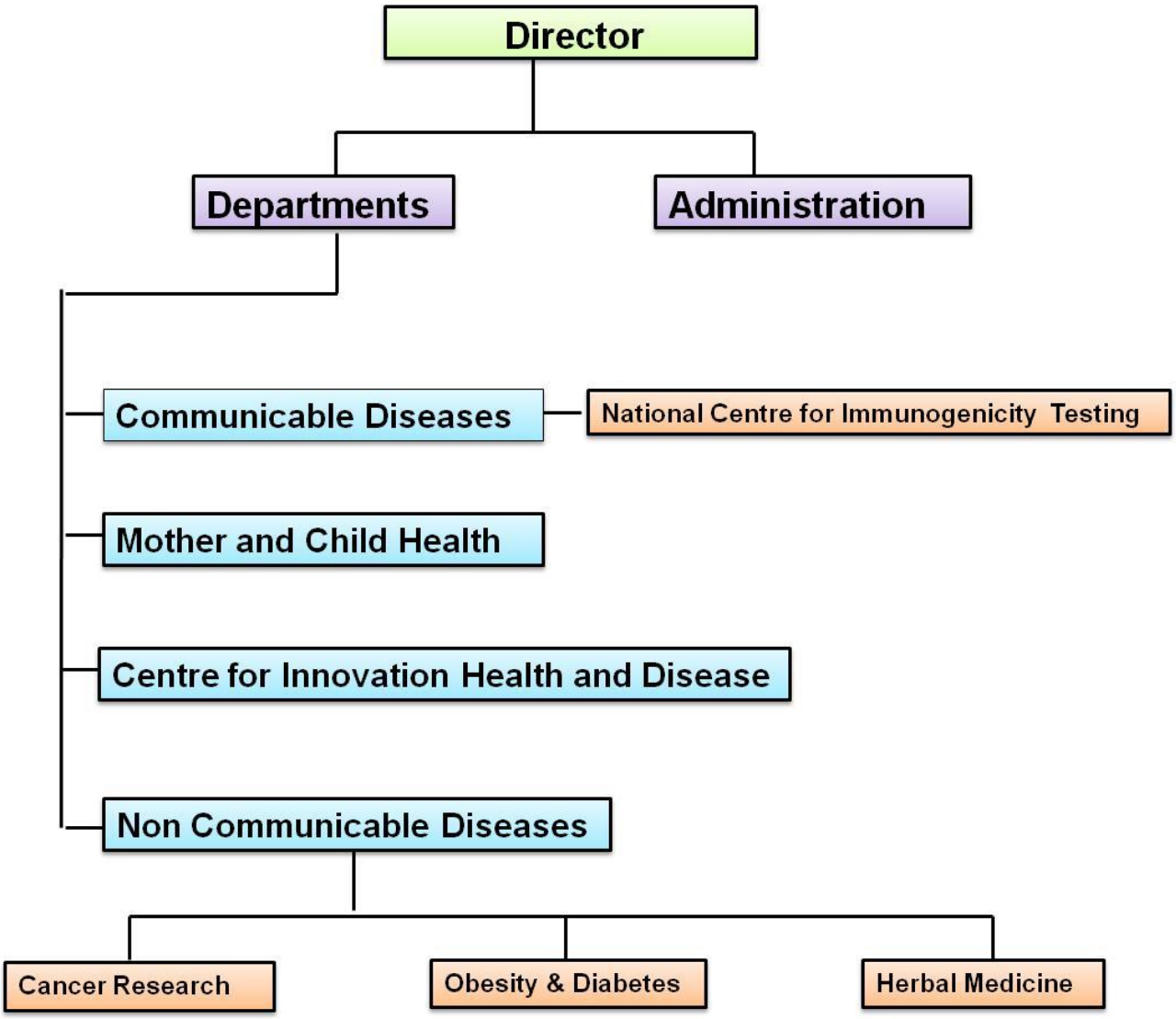
Several activities had been organized at the institute and also the staff and students participated in national and international events. A brief summary of these events, activities and achievements by all the staff members has been presented in the current report.

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

Organogram


Director
Departments
Administration
Communicable Diseases
National Centre for Immunogenicity Testing
Mother and Child Health
Centre for Innovation Health and Disease
Non Communicable Diseases
Cancer Research
Obesity & Diabetes
Herbal Medicine

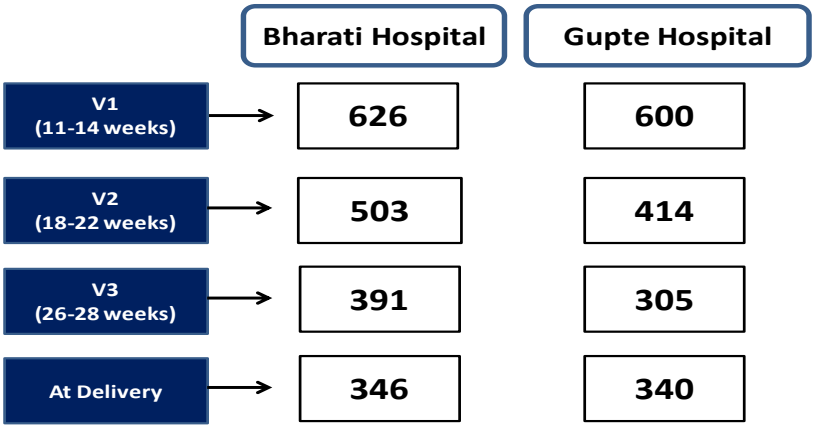
Name of the Programme: Mother and Child Health

1. Title: Investigating Mechanisms Leading to Preeclampsia; **(Project ID: MC/17/1/E)** **Funding**: ICMR Centre for Advanced Research; **Duration:** March 2017 to March 2022; **Sanctioned Amount**: 705.00 Lakhs; **Investigators**: PI- Dr. Sadhana Joshi; Co PI- Dr. Girija Wagh, Dr. Sanjay Lalwani, Dr. Sanjay Gupte; **Co-Investigators-** Dr. Giriraj Chandak; Dr. Savita Mehendale, Dr. Arun Kinare, Dr. Priscilla Joshi, Dr. Manjiri Karandikar, Dr. Leena Srivastav, Dr. Hemant Mandke, Dr. Anvita Kale, Dr. Deepali Sundrani, Dr. Nisha Wadhwani; **Ph.D. Students:** Vaishali Kasture (DST Inspire SRF); Juhi Nema (CSIR-JRF); Anjali Jadhav (ICMR-SRF); Kinjal Dave (CSIR-JRF); **Human Ethical Approval:** IEC/2016/54; **Animal Ethical Approval:** BVDU/IRSHA/2017-2018/582

Background: The current study aims to understand the risk factors and underlying mechanisms leading to preeclampsia. The studies carried out under this CAR will be useful in development/validation of biomarkers for early prediction of preeclampsia. It will also help in understanding the neurodevelopmental outcome of children born to women with preeclampsia.

Work done: Recruitment and Follow up of Subjects: The recruitment and follow up of patient is on-going. The total number of subjects recruited at each time point at both the hospitals is as follows (Fig. 1).

Figure 1: Recruitment of Study Participants till date at both the Hospitals



Information Recorded: Maternal age, BMI, education, and obstetric history was recorded. Data on socioeconomic status of the subjects was collected using the standard of living index (SLI). A quantitative food frequency questionnaire (FFQ) (one month recall) was administered at three different time points i.e. 11-14 wks, 18-22 wks, 26-28 wks, to estimate the frequency of consumption of different food items. A 24 hour recall questionnaire was also administered across gestation at three different time points i.e. 11-14 wks, 18-22 wks, 26-28 wks. The women's physical activity was recorded at three time points (11-14 wks, 18-22 wks, 26-28 wks) using simple numeric measures in a specially designed activity questionnaire arranged in 3 main
domains – occupation, travel and leisure activities.

Sample Collection: Maternal blood was collected and processed at four different time points (11-14 wks, 18-22 wks, 26-28 wks, and delivery) from each subject. Similarly, cord blood and placenta was also collected and processed at delivery. Different aliquots of plasma, erythrocyte, lymphocyte, serum and placenta are stored in different -80°C freezers.

Biorepository: Biorepository is being established with this project (Fig 2).
Figure 2: Biorepository of the ICMR CAR Study

Preliminary Findings: Maternal Characteristics: Maternal age, weight, height, BMI and systolic and diastolic blood pressures were higher in women recruited from Gupte hospital as compared to those recruited at Bharati hospital.

Education Level of the Women and their Spouse: Majority of the women recruited were either post graduates/graduates. Between the two hospitals, it was observed that higher percent of pregnant women and their spouse at Gupte hospital had higher level of education as compared to women and their spouse at Bharati hospital.

Occupation of the Subject and their Spouse: Hospital wise comparison revealed that higher percent of pregnant women and their spouse at Gupte hospital were professionals. Most of the women at Bharati hospital were housewives.

Mode of Conception: We observed that the percent women with natural conception were higher as compared to IVF and IUI at both the hospitals.

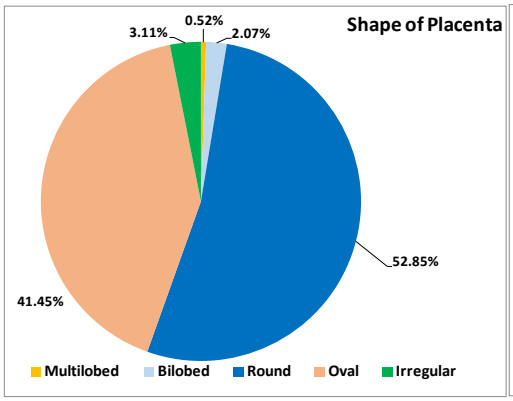
Food Frequency Questionnaire Assessment: The frequency of consumption of food groups, such as beverages, roti, rice, green leafy vegetables ($p<0.01$, for all) and non-vegetarian ($p<0.05$) was higher in Bharati Hospital as compared to Gupte hospital. However, the consumption of food groups, viz. salad, fruits, milk products, fermented foods, snacks, festival food and dal ($p<0.01$, for all) were higher at Gupte Hospital.

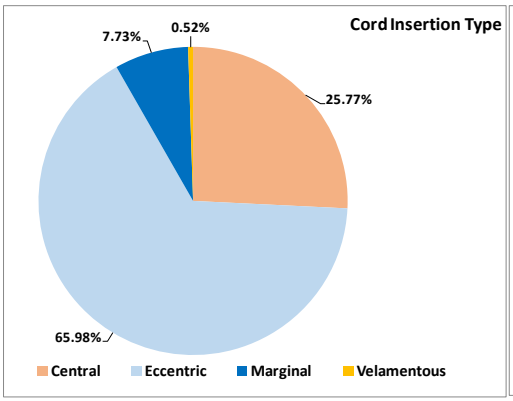
Color Doppler and Ultrasonography Assessments: Color Doppler and ultrasonography (USG) assessments were carried out at 11-14 wks, 18-22 wks and at 32-35 wks of gestation. All measurements were in accordance with the International Society of Ultrasound in Obstetrics and Gynecology (ISCOG) and Fetal Medicine Foundation (FMF) protocols (ISCOG guidelines, UOG, 2013). All measurements were similar in both the hospitals.

Placental Characteristics: Placental characteristics like shape, dimension, thickness, cord insertion type, etc have been recorded for all the placentas that have been delivered till date. Figure 3 shows the percentage of various placental shapes and cord insertion types for all the placentas that have been delivered till date at both the hospitals.

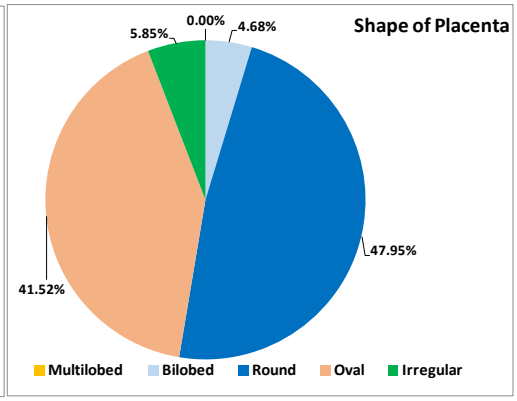
Figure 3: Placental Shape and Cord Insertion Type

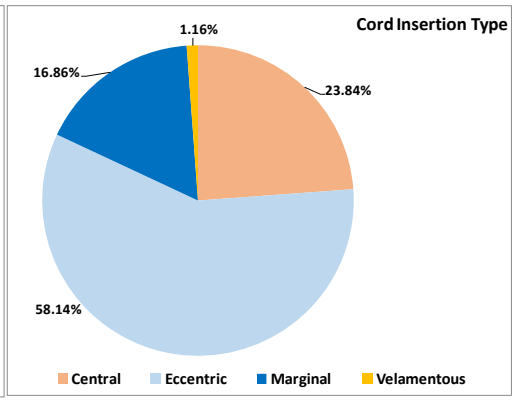
Bharati Hospital





Gupte Hospital





Placenta Histology: A total of 345 placenta samples have been processed, examined and archived (block and slides) in the Dept. of Pathology, Bharati Vidyapeeth Medical College under the guidance of Dr. N.S. Mani.

Infant Characteristics at Birth: Neonatal measurements such as baby weight, length, head circumference and chest circumference for all the neonates were recorded at birth and were found to be similar between both the hospitals.

Children Follow Up: Follow up of children for anthropometric measurements at various time points has been initiated. The children are followed up as per the vaccination routine/schedule at 6 wks, 10 wks, 14 wks, 6 months, 9 months, 12 months, 15 months, 18 months and 24 months as per the hospital practice. A total of 185 (80%) were followed at 6 weeks of which 49 children are yet to reach the first time point i.e. 6 weeks at Bharati hospital. A total of 169 (78%) were followed at 6 weeks of which 55 children are yet to reach first time point i.e. 6 weeks at Gupte hospital. The subsequent follow up of children at various time points is ongoing.

Biochemical Analysis: Samples are being analyzed for the biochemical parameters like one carbon metabolites (folate, vitamin B_{12}, homocysteine, fatty acids), vascular endothelial growth factor (VEGF), soluble fms-like tyrosine kinase-1 (sFlt-1), placental growth factor (PlGF), vitamin D and thromboxane B2.

Methylation Study: A total of 200 previously collected and stored samples (100 controls and 100 preeclampsia) at IRSHA were used to investigate methylation patterns of candidate genes in the placenta. Methylation analysis of *PlGF*, *HIF3A* and *FLT-1 and PEMT* genes has been initiated.

Bioinformatics Analysis: Bioinformatic analysis of the selected genes was carried out using various regulatory feature tracks like DNase cluster and histone markers in UCSC genome browser (http://www.genome.ucsc.edu/) as well as other independent tools like CTCFBSDB, MEME etc. (Fig 5).

Figure 5: Bioinformatic Analysis of Placental Growth Factor (PlGF) Gene

Genomic sequences for pyrosequencing assay design were extracted from the UCSC genome browser (http://www.genome.ucsc.edu/) and primers (both biotin labelled and unlabelled) were designed using Pyromark assay design software 2.0. The primers for all the genes were tested and PCR conditions were standardized. The bisulphite-modified DNA was used for gene-specific methylation analysis by the PyroMark Q24 (Cat No./ID: 9001514, Qiagen, Hilden, Germany).

Conclusions summarizing the achievements of the methylation work

This pilot study shows differential methylation of *PlGF* and *HIF3A* genes between the normotensive and preeclampsia groups. Gene specific methylation analysis of selected candidate genes report signififcant hypermethylation in the *HIF3A* region and significant hyomethylation at various CpG sites in the *PlGF* promoter region. Our data indicates disturbed methylation patterns of genes regulating the process of placental angiogenesis in women with preelampsia.

Animal Study

This study was approved by the Bharati Vidyapeeth Animal Ethical Committee (IAEC/ CPCSEA/ BVDUMC/2670/2017/002/016) on 24/03/2017.

Study Design: Pregnant rats were divided into a total of 5 groups (Control, early onset preeclampsia (EOP); late onset preeclampsia (LOP); early onset preeclampsia supplemented with omega-3 fatty acid and vitamin E and late onset preeclampsia supplemented with omega-3 fatty acid and vitamin E. Early onset preeclampsia was induced by administering nitric oxide synthase inhibitor L-NAME (Sigma Chemical Co., St. Louis, MO) by oral gavage at a dosage of 50 mg/kg/d from d7 to d19 of gestation. In case of late onset preeclampsia L-NAME was administered from d14 to d19 of gestation.

Results:

Placental protein levels and mRNA levels of VEGF were lower in both early onset preeclampsia and late onset preeclampsia groups; whereas supplementation of omega-3 fatty acids and vitamin E was beneficial only in case of the late onset preeclampsia group in improving the VEGF levels (Figure 6).

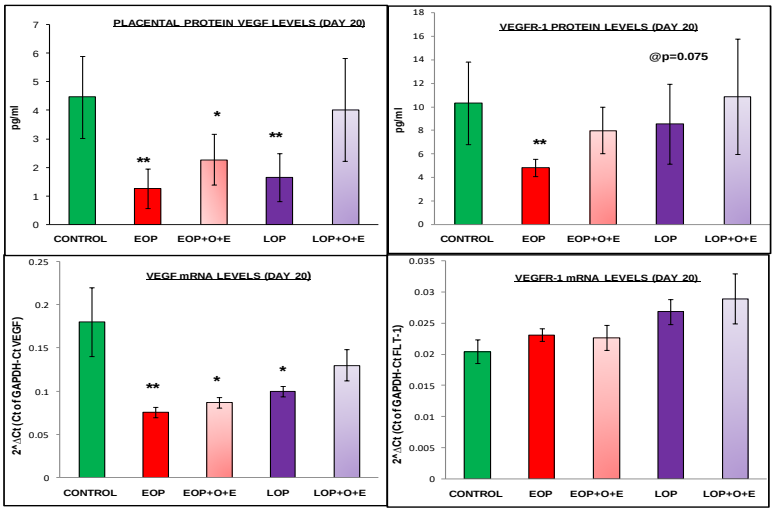
VEGFR-1 protein levels were lower only in the early onset preeclampsia group and supplementation was not beneficial in improving the VEGFR-1 levels (Figure 6).

Placental HIF-1α mRNA levels were higher only in the early onset preeclampsia group; supplementation was beneficial in normalizing the HIF-1 α mRNA levels. (Figure 7).

Supplementation increased the protein levels of PPAR-g in the LOP group. (Figure 7).

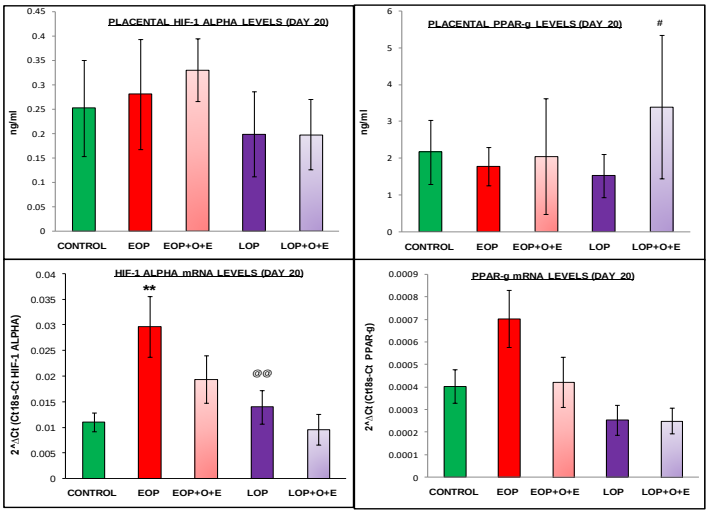
Maternal plasma MDA levels were higher in the early onset preeclampsia group as compared to control and late onset preeclampsia groups, and supplementation to this group (EOP+O+E) resulted in reduced MDA levels as compared to early onset preeclampsia.

Figure 6: Placental protein and mRNA levels of VEGF and VEGFR-1 at day 20 of gestation



Values are expressed as Mean ± SD (for protein levels) and Mean ± SEM (for mRNA levels); **p<0.01, *p<0.05 as compared to control, $^{@}$p=0.075 as compared to EOP.
Dietary Groups: Control (C); Early onset preeclampsia (EOP); Early onset preeclampsia supplemented with Omega-3 Fatty Acids and Vitamin E (EOP + O + E); Late onset preeclampsia (LOP); Late onset preeclampsia supplemented with Omega-3 Fatty Acids and Vitamin E (LOP + O + E)

Figure 7: Placental protein and mRNA levels of HIF-1 Alpha and PPAR-g at day 20 of gestation



Values are expressed as Mean ± SD (for protein levels) and Mean ± SEM (for mRNA levels); **p<0.01 as compared to control, @@p<0.01 as compared to EOP, #p<0.05 as compared to LOP. Dietary Groups: Control (C); Early onset preeclampsia (EOP); Early onset preeclampsia supplemented with Omega-3 Fatty Acids and Vitamin E (EOP + O + E); Late onset preeclampsia (LOP); Late onset preeclampsia supplemented with Omega-3 Fatty Acids and Vitamin E (LOP + O + E)

2. Title: Early Interventions to Support Trajectories for Healthy Life in India (EINSTEIN). Healthy Life Trajectories Initiative (HeLTI) (**Project ID:** MC/17/2/E) Multicentric Project
Funding: DBT; **Sanctioned Amount:** Total Sanctioned Rs. 743.44 Lakhs; IRSHA Share: Rs.13.50 Lakhs; **Duration:** Dec 2017 to Nov 2020; **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: A community engagement process was initiated by meeting village elders/local leaders, the village women and men, local government officials and the local health workers to explain the study and obtain their support. The project was well received and people were keen to participate.
After recruitment of research and community health staff, they have been trained in basic research methods, data collection, and Healthy Conversation Skills. Healthy Conversation Skills (HCS) was developed by our collaborators in Southampton and is a communication technique designed to support behavior change; HCS will underpin all communication with participants. The 105 study villages have been identified and been mapped by field workers. Enumeration of eligible women has been completed in 72 of 105 villages. Qualitative work to develop the intervention materials and mode of delivery is nearly complete; we have conducted focus groups with village women, husbands, mothers/mothers-in-law, village leaders and officials, and health workers. In the focus groups, we explored their perspectives on the benefits and challenges of the intervention; local issues that impact the health of young women and their families; what could be done to improve health; perceptions of pregnancy; aspirations for their children; and current maternal and child health practices.
Harmonisation work with the other HeLTI country teams is in place for intervention development, data collection, biospecimen collection and processing, and governance arrangements.
3.Title: Pro-neurotrophins /p75NTR Signalling Contributes to Increased Apoptosis in Preterm Placentae (**Project ID:** MC/17/3/E)
Funding: DST-SERB; **Sanctioned Amount**: 40.48 Lakhs; **Duration:** June 2017 to June 2020; **Investigators:** PI: Dr. Preeti Chavan Gautam; **Co-Investigators**: Dr. Sadhana Joshi; **Human Ethical Approval:** IEC/2017/11
Biochemical and molecular analysis is ongoing

4.Title: Influence of Maternal One-carbon (1C) Metabolism in Placental Function, Fetal Growth and Programming (**Project ID:** MC/18/4/E) Multi-Institutional

Funding: DBT; **Sanctioned Amount**: Total Sanctioned Rs. 170.00; IRSHA Share: Rs. 68.5; **Duration:** March 2018 to Feb 2021; **Principal Investigator at IRSHA:** Dr. Sadhana Joshi; **Human Ethical Approval**: IEC/2018/44

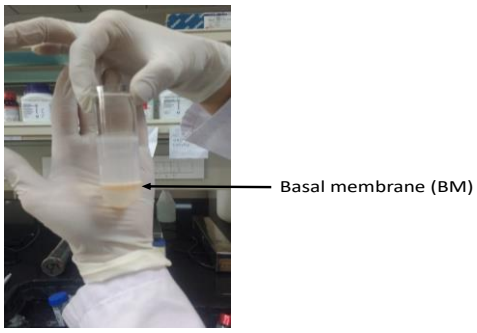
Background: The primary goal of this proposal is to examine the influence of maternal 1C metabolism on placental structure and function and understand the molecular mechanisms underlying these events.

Work done: Recruitment of Study Subjects and Sample Collection

In the current year, recruitment of patients at Bharati hospital was completed and a total of 101 subjects (52 normotensive control and 49 preeclampsia) were recruited till date. From these subjects, samples like maternal blood at delivery, cord blood and placenta tissue were collected, processed and stored at -80ºC.

Isolation of Placental Plasma Membranes: The above stored placental homogenates were used for the isolation of placental syncytiotrophoblast basal and microvillous plasma membranes. A total of 25 samples have been processed for isolation of these plasma membranes [(basal membrane (BM) and microvillous membrane (MVM)] which are snap frozen and stored in aliquots in -80^{0}C.

Figure 8: Isolation of Basal Membrane Fraction using Sucrose Gradient



Purity of Isolated Membranes: The following markers are used to assess the purity of the membranes, and the enrichment in purified membrane fraction is obtained by comparing with the placental homogenates.

a) Microvillous Membrane (MVM) Alkaline Phosphatase Activity: The mean enrichment of alkaline phosphatase in MVM is 23.28±7.98.

b) Basal Membrane (BM) VDAC1 Protein Expression: The mean enrichment of VDAC1 expression in BM is 37.44 ± 24.68.

Expression of Nutrient Transporters in Isolated Membranes: Western blot analysis for fatty acid transporters (FATP-2 and FATP-4) in the MVM and BM of control and preeclampsia placental samples is initiated and analysis is on-going.

Fatty Acid Analysis: Maternal plasma fatty acid analysis for KEM and Bharati samples has been initiated and analysis is on-going.

6.Title: Placental Lipid Transport and Fetal Growth in Preeclampsia **(Project ID**:MC/18/1/RA)

Funding: Indian Council of Medical Research; **Duration:** Sept 2018- Sep 2021; **Sanctioned Amount**: 14.42 Lakhs; **Investigators:** Dr. Amrita Khaire, Dr. Sadhana Joshi, Dr. Girija Wagh; **Human Ethical Approval:** BVDUMC/ IEC/ 33A

Background: The current proposal aims to examine the placental lipid profile and its association with growth measures of the neonates in preeclampsia. The expression of genes involved in placental lipid transport will also be investigated.

Objectives

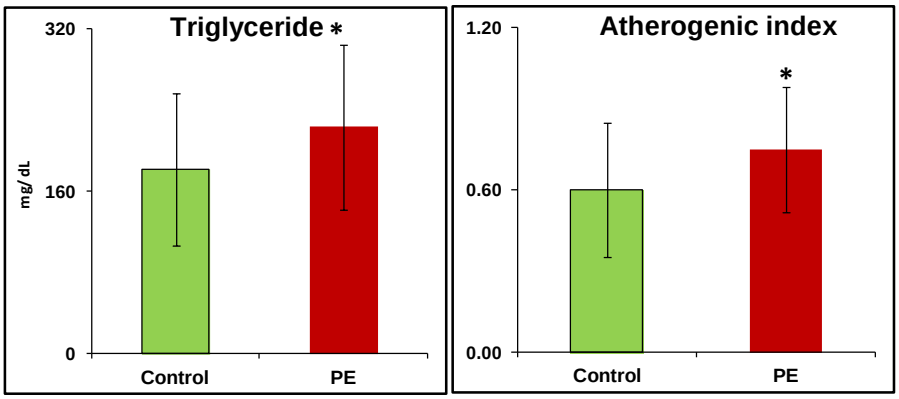
- To compare placental lipid profile in normotensive control women and women with preeclampsia
- To examine expression pattern of genes involved in placental lipid transport (low density lipoprotein receptor (LDL-R) and apolipoprotein B (Apo B) in the above women
- To analyze the association of placental lipid profile and genes involved in lipid transport with anthropometric measurements at birth in neonates born to normotensive control mothers and mothers with preeclampsia.

Work done: Analysis of plasma lipid levels (total cholesterol, triglyceride, HDL, LDL) from 30 normotensive and 30 women with preeclampsia. Standardization for mRNA expression of apolipoprotein B and lipoprotein lipases

Results:

- Higher levels of plasma triglycerides and atherogenic index in women with preeclampsia compared to normotensive control women (Fig. 10).
- A positive association of maternal triglycerides and VLDL with diastolic blood pressure in the whole cohort.
- A negative association of maternal HDL with systolic blood pressure in the control group while a positive association of maternal HDL with systolic blood pressure in the preeclampsia group.
- A negative association of maternal triglycerides. VLDL, atherogenic index and Apo B: Apo A with baby weight in the whole cohort.

Figure 10: Plasma lipid Profile in the preeclampsia and control groups



*p<0.05 compared to control

Conclusion: The findings of the present study indicate that preeclampsia is associated with hypertriglyceridemia and higher atherogenic index which are considered as major risk factors of cardiovascular diseases. There was also a trend for higher lipid: lipoprotein ratios of ApoB:Apo and cholesterol:HDL in women with preeclampsia which needs to be validated on a large cohort. We observed a negative association of maternal triglycerides. VLDL, atherogenic index and Apo B: Apo A with baby weight

7.Title: Epigenetic regulation of placental peroxisome proliferator activated receptor (PPAR) in women delivering low birth weight babies (**Project ID:** MC/19/5/E)
Funding: DBT BioCARe; **Sanctioned Amount:** 35.50 Lakhs; **Duration:** April 2019 to April 2022; **Investigators:** **PI-** Dr. Deepali P. Sundrani **Co-Investigators:** Dr. Sadhana Joshi; Dr. Tushar Panchanadikar

Background: Low birth weight (LBW) babies are associated with fetal and neonatal morbididty and motality and are at increased risk for non-communicable diseases in later life. However, the molecular determinants of LBW are not well understood. Early life exposures like altered maternal nutrition may have long-lasting effects on health via epigenetic mechanisms like DNA methylation and non-coding RNA regulation. The placenta is known to play a key role in 'programming' the fetus for risk of diseases in later life. Peroxisome proliferator-activated receptor (PPAR) is a key transcription factor that regulates placental angiogenesis and influences pregnancy outcome. The activity of PPAR is regulated by ligands such as long chain polyunsaturated fatty acids. This study for the first time aims to understand the molecular mechanisms (DNA methylation and microRNA regulation) underlying the association of maternal fatty acid status and PPAR in the placenta in women delivering LBW babies.

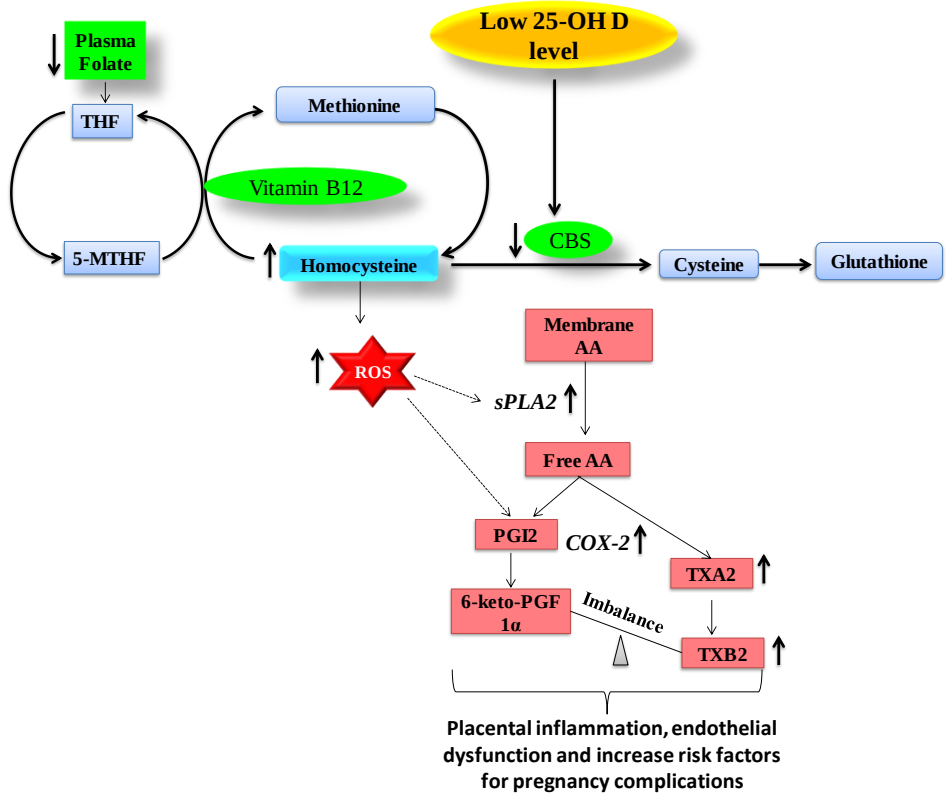
Work Done: The project was sanctioned on 26th April 2019 and a candidate for the post of Project Assistant was recruited.
Recruitment of patients at Bharati Hospital was initiated. Till date we have recruited 97 subjects (74 women delivering normal birth weight baby and 23 women delivering low birth weight baby).
Subjects history and clinical information and neonatal characteristics have been recorded

Placenta and maternal blood samples at delivery are collected, processed and stored at -80℃ Maternal blood samples are layered on histopaque and centrifuged at 1800 rpm for 35 min to separate the plasma and erythrocytes. The erythrocyte fraction is washed 3 times with normal saline. Then, the plasma and erythrocyte aliquots are stored at -80°C until further analysis.

8.Title: Association of Vitamin D Status and Long Chain Polyunsaturated Fatty Acid Metabolism in Preeclampsia (**Project ID:MC/19/1/P)**
Sanctioned Amount: 13.70 Lakhs; **Duration:** April 2019 to April 2022;
Funding: UGC; **Guide**: Dr. Sadhana Joshi; **PhD Student**: Anindita Nandi (UGC JRF/SRF)

Animal study
Result of animal study indicate that, maternal vitamin D deficiency influences fatty acid metabolism and the inflammatory eicosanoids production which may lead to adverse pregnancy outcome. Our results suggest that vitamin D and fatty acids may work in concert to regulate fetal growth (Fig 9).

Figure 9: Effect of vitamin D deficiency on fatty acid metabolism through one carbon cycle



AA-arachidonic acid, sPLA2-secreted phospholipase A2, PG-prostaglandin, TX-thromboxane, COX-cyclooxygenase, CBS- cystathionine-β-synthase, THF-tetrahydrofolate, 5-MTHF-5-methyltetrahydrofolate, ROS- reactive oxygen species
Human study
A total of 119 pregnant women [69 normotensive control (NC) and 50 women with PE] were recruited at delivery after taking written consent from each patient. Maternal blood, cord blood and placenta collected at delivery.

Results

Maternal 25(OH)D levels were negatively associated with maternal systolic and diastolic BP ($p<0.01$ for both). Maternal and cord serum 25-hydroxyvitamin D [25(OH)D] levels were lower ($p<0.01$for both) in women with PE compared to NC women. Maternal plasma total polyunsaturated fatty acids (PUFA) levels were lower ($p<0.05$) while levels of total saturated fatty acids (SFA) and total monounsaturated fatty acids (MUFA) were higher ($p<0.05$ for both) in women with PE. Cord erythrocyte PUFA levels were higher ($p<0.01$) in PE women. Maternal 25(OH)D levels were positively associated with maternal total PUFA ($p<0.01$) and negatively associated with maternal total SFA ($p<0.05$), total MUFA ($p<0.01$).

9.Title: Investigating the role of enzymes regulating the one carbon metabolism in preeclampsia (Project ID: MC/19/2/P)

Funding: Indian Council of Medical Research (Senior Research Fellowship to Anjali Jadhav); **Sanctioned Amount:** 13.70 Lakhs; **Duration:** April 2019 to April 2022;

Guide: Dr. Sadhana Joshi; **PhD Student**: Anjali Jadhav (ICMR /SRF); **Human Ethical Approval:** Institutional Ethics no. : IEC/ 2018/ 44; **Animal Ethical Approval**: IAEC/ CPCSEA/2311

Background: Preeclampsia is a pregnancy-specific disorder characterized by new-onset hypertension in combination with proteinuria after 20 weeks of gestation. A significant number of studies have shown that adverse influences during the development of the fetus play an important role in determining the risk of cardiovascular disease in adult life. During pregnancy nutritional demands are increased and influence the health of the pregnant woman as well as the growing fetus. Studies have shown that maternal nutrition not only influences pregnancy outcome but can also influence epigenetic patterns which 'programs' the fetus for diseases in adulthood. Maternal micronutrients such as folic acid and vitamin B_{12} involved in the one-carbon metabolism are reported to have an effect on DNA methylation pattern. In the one carbon cycle, folate and vitamin B_{12} are involved in the transfer of methyl groups to SAM (s-adenosyl methionine) which is a major methyl group donor for methylation reactions. The enzymes methylene tetrahydrofolate reductase (MTHFR) methionine synthase (MS/MTR) and methionine adenosyl transferase (MAT) play a critical role in regulating the one carbon cycle.

Our earlier studies in women with preeclampsia have reported an altered one carbon cycle, reduced omega-3 fatty acids and increased homocysteine and oxidative stress. It is likely that these changes in the maternal micronutrients and long chain polyunsaturated fatty acids (LCPUFA) could influence the regulation of enzymes involved in the one carbon metabolism which may further affect the methylation pattern. The current study plans to examine the levels of enzymes regulating the one carbon cycle in the placenta of women with preeclampsia and compare them with normotensive women. Further, the effect of maternal micronutrient supplementation on the enzymes will be examined using an animal model

Objectives of the Animal Study

To examine the effect of micronutrients (folic acid and vitamin B_{12} and omega-3 fatty acids) supplementation on the one carbon cycle enzymes in a rat model of pregnancy induced hypertension

Objectives of the Human Study

To analyze placental gene expression levels of key enzymes (MTHFR, MS, MAT)of the one carbon metabolism in women with preeclampsia and compare them with normotensive control women

To examine the association of expression of these enzymes with maternal nutrients (folic acid, vitamin B_{12} and omega-3 fatty acids)

Work done: Pregnant Wistar rats (n=8) in each group were assigned randomly to control and five treatment groupsThe treatment groups included 1) PIH 2) PIH +vitamin B_{12} (0.5µg/Kg diet) supplementation 3) PIH + folic acid (0.8mg/Kg diet) supplementation 4) PIH + Omega-3 fatty acid (ω3/ ω6 ratio; 1:1) supplementation and 5) PIH + combined micronutrient supplementation (vitamin B_{12} + Folic acid + omega-3 fatty acid). The mRNA levels of MTHFR, MAT2A and MS were estimated from the placental tissue samples using RT-PCR

Results

- MTHFR levels: The MTHFR mRNA levels were comparable between control and PIH group. However, it was higher ($p<0.05$) in PIH+combined supplementation group (vitamin B_{12}, folate and omega-3 fatty acid) as compared to control group and PIH groups.
- MAT2A levels: There was no significant difference between the levels of MAT2A gene in PIH group when compared with control. However, MAT2A mRNA levels were significantly higher in PIH+omega-3 fatty acid supplemented group as compared to PIH group.
- MTR (MS) level: The MTR enzyme mRNA levels were comparable to control in all the groups.

Name of the Programme: Cancer Research

1. **Title:** Evaluating the anticancer activity of homeopathic potencies of Terminalia chebula (TC) in breast cancer cell lines and analyzing the best potency for activity in breast cancer mouse model. (**Project ID:** CR/16/1/E)
Funding: EMR, AYUSH CCRH; **Duration:** December 2016-December 2019; **Sanctioned Amount:** 42.98 lakhs; **Investigators:** PI- Dr. Ruchika Kaul-Ghanekar; **Co-PI**- Dr. Nilesh Shah (Homeopathy College, BVHC); **Ph.D. Students:** Dr. Nilesh Shah (Homeopathy College, BVHC); **Animal Ethical** Approval: BVDUMC/1883/2018/002/012

Background: Breast cancer is the most common cancer diagnosed among women and is the leading cause of cancer death. Homeopathic medicines are given as a supportive therapy for the same. Homeopathic preparations of TC could reduce the viability of breast cancer cell lines without affecting the non-cancerous cells that has been recently reported by our lab. Based on that study, the present study is focused to evaluate the anti-cancer activity of other potencies i.e. MT, 3X, 3C, 6C, 30C, 200C, 1M, 10M, 50M and CM on breast cancer cell lines MCF-7 and MDA-MB-231 and noncancerous breast epithelial cell line MCF10A.
Work done: The in vitro studies showed that 6C and 50M potencies of Terminalia chebula showed potent anticancer activity. Hence 6C and 50M were taken further for acute oral toxicity and dose range finding (DRF) studies in Swiss albino mice.
Results: The potencies 6C and 50M were evaluated for their safety in Swiss albino mice by acute oral toxicity study followed by dose-range finding (DRF) study according to the OECD 423 guideline. Both the potencies tested at 1:10 dilution for acute were found to be safe in animal model.6C potency was selected for the DRF study and found to be safe in Swiss albino mice at 1:20, 1:40 and 1:80 dilutions for7 consecutive days oral dosing. No significant difference was observed in the body weight, food consumption, haematological, biochemical and histo-pathological parameters of treated mice compared to the control mice.
Conclusion: The potency '6C' has been found to be safe for in vivo study hence it can be further used to evaluate its tumor retardation potential in breast cancer mouse model.

2. **Title:** Evaluating the anticancer activity of homeopathic preparation of Linum usitatissimum in breast cancer cell lines (**Project ID:** CR/18/2/E)
Funding: EMR, AYUSH CCRH; **Duration:** October 2018-October 2021; **Sanctioned Amount:** 42.02 lakhs; **Investigators: PI-** Dr. Prerna Raina; **Co-PI**- Dr. Swati Shinde; **Ph.D. Students**: Ms. Rupika Pawar

Background: Breast cancer is the second leading cause of cancer death in women worldwide. The conventional treatments for breast cancer such as chemotherapy, hormone therapy and radiotherapy have limitations as sever toxicity, resistance and relapse. Complementary and Alternative Medicines (CAM) are widely studied as an adjunct to conventional treatment. Homeopathic treatment is one of CAMs being used for management of cancer. The proposed study involves evaluation of anticancer activity of homeopathic

potencies of L. usitatissimum (LU) against breast cancer. L. usitatissimum commonly known as Flax seeds or Lin seed has been used as a beneficial nutritional supplement in management of various disorders which includes arthritis, obesity and other inflammatory disorders. The existing literature reports the inhibitory effects of extracts from LU on cell vitality, proliferation and cytotoxicity of breast cancer cell lines. However, anticancer activity of homeopathic potencies LS have not been reported.

Work done: The effect of different potencies of homeopathic preparation of Linum usitatissimum (LU) on viability of breast cancer cell lines MDA-MB-231 and MCF-7 was evaluated.

Results: The effect of homeopathic potencies (6C, 30C, 12C, 200C and 1M) of Linum usitatissimum was evaluated on the viability of MDA-MB-231 and MCF-7 breast cancer cells. The potencies significantly reduced the viability of both MDA-MB-231 and MCF-7 cells at 1:12.5 dilutions. In MDA-MB-231, at 1:12.5 dilution 45.7 ± 1.3%; 37.4 ± 5.4%; 30.3 ± 6.9%; 28.3 ± 3.7%; 54.6 ± 14.3% viability was observed in the cells treated with 6C, 30C, 200C, 12C and 1M potencies of LU, respectively. On the other hand, in MCF-7 at 1:12.5 dilution, 42.9 ± 17.2%; 59.1 ± 18.5%; 54.4 ± 17.4%, 47.7 ± 10.7% and 48.9 ± 0.9% viability was observed in cells treated with 6C, 30C, 200C, 12C and 1M potencies of LU, respectively.

Conclusion: The homeopathic potencies of Linum usitatissimum significantly reduced the viability of breast cancer cell lines, MDA-MB-231 and MCF-7.

3. Title: Evaluating the anticancer activity and mechanism of action of Unani formulation Habbe Musaffi Khoon (HMK) against cervical cancer (**Project ID**: CR/18/3/E)
Funding: EMR, AYUSH CCRM; **Duration**: September 2018- September 2021; **Sanctioned Amount**: 57.56 lakhs; **Investigators: PI-** Dr. Ruchika Kaul-Ghanekar; **Co-PI-**Dr Gazalla Mulla, Dr Prerna Raina; **Ph.D. Students**: Ms Nidhi Sharma

Background: Cervical cancer is the fourth most frequent cancer in the women in the world. The 5-year prevalence of cervical cancer in India has been estimated to be 2,25,689 and 1474265 in the world (IARC 2018). Hence cervical cancer is an important public health problem that needs urgent intervention. Despite advanced treatment methods, the associated adverse events, recurrence and resistance continue to persist. Hence Complementary and Alternative Medicine (CAM) are being studied worldwide. The Unani System of Medicine is one of the CAM, which is based on balancing the body humors which can be used as an alternative approach in treatment of cervical cancer. Habbe Musaffi Khoon is a compound formulation and well known blood purifier. The scientific studies have reported anticancer/antioxidant activity of number of individual components of Habbe Musaffi Khoon. Therefore, it can be hypothesized that it can be a potential formulation against cervical cancer.

Work done: The effect of Habbe Musaffi Khoon on viability of cervical cancer cell lines HeLa and SiHa was studied.

Results: The effect of aqueous extract of Habbe Musaffi Khoon was evaluated at concentrations 0, 20, 40, 80, 160, 320, 640, 1280 µg/ml on the viability of cervical cancer cell lines, HeLa and SiHa, using MTT assay. It significantly decreased the viability of HeLa and SiHa cells (Fig 5). The IC-50 value was found to be ~320 µg/ml ($p<0.0001$) for HeLa and SiHa.

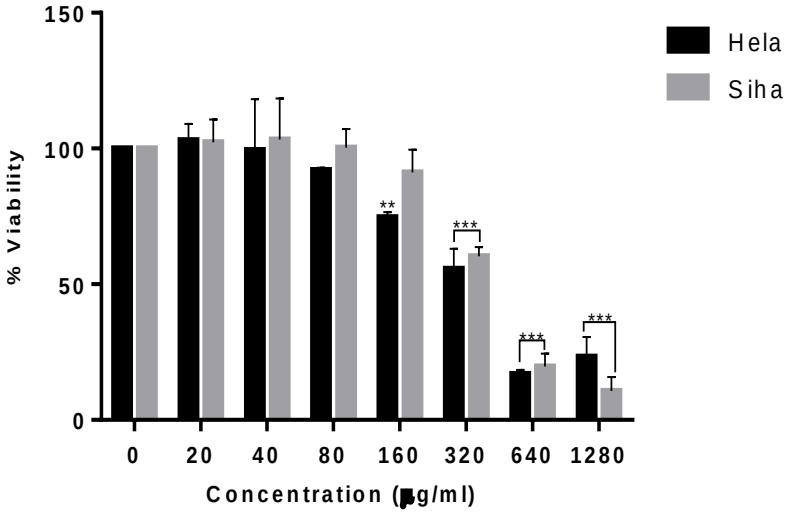


Figure5. Habbe Musaffe Khoon (aqueous extract) altered the viability of cervical cancer cell lines. The extract showed significant decrease in viability of HeLa at 160 µg/ml ($p<0.01$). and SiHa at 320 µg/ml ($p<0.001$). All the date have been presented as mean ± SD. **$p< 0.01$, ***$p<0.001$ indicates statistically significant differences compared to the control untreated group.

Conclusion: Habbe Musaffe Khoon (aqueous extract) shows potential anticancer activity against cervical cancer cells SiHa and HeLa.

3.**Title:** Evaluating the effect of Alpha Linolenic acid, an omega-3 fatty acid on the modulation of epigenetic markers in Cervical cancer cells (**Project ID:** CR/18/4/E)
Funding: DST SERB; **Duration:** October 2018- October 2021; **Sanctioned Amount:** 33.16 Lakhs; **Investigators: PI**- Dr. Ruchika Kaul-Ghanekar; **Co-PI-** Dr Preeti Gautam-Chavan; **Ph.D. Students**: Ms Amrita Ulhe

Background: Cervical cancer is the second major cause of cancer related death in the women all over the world. Oncogenic human papillomavirus (HPV) is the major cause of development of cervical cancer. Nutrition has been shown to play an important role in the regulation of various cancers. Dietary fat, particularly, omega 3 fatty acids have been reported to suppress the transformative and inflammatory processes that initiate carcinogenesis. ALA, an essential omega-3 fatty acid is mainly present in green leafy vegetables, oil, seeds (flaxseed, canola, perilla), nuts. It has been reported to exhibit anti-cancer activity against breast, colon and esophageal cancer cell lines. We have recently shown that ALA modulated the growth of cervical cancer cell lines through regulation of NO

release, induction of lipid peroxidation, apoptosis via caspase 3 activation. ALA modulated the growth kinetics of cervical cancer cells, reduced cell migration with decrease in the expression of VEGF, MMP-2, and MMP-9 proteins. Besides this, ALA decreased the expression of phosphorylated p38, pERK1/2, c-JUN, NFκB, and COX2, proteins. Most importantly it reduced the expression of HPV onco-proteins E6 and E7, thereby restoring of expression of tumor suppressor proteins, p53 and Rb. Since ALA has exhibited anti-neoplastic potential in cervical cancer, in the current project, we want to elucidate the potential of ALA to induce epigenetic alterations that would help in the prevention of cervical cancer.

Work done: The effect of ALA on viability of cervical cancer cell lines SiHa and HeLa was evaluated by MTT assay. The effect of ALA on global DNA methylation was studied by evaluating the expression of Histone deacetylases-1 (HDAC1) by real time PCR.

Results: The effect of alpha linolenic acid (ALA) on the viability of SiHa and HeLa cervical cancer cell lines was determined by MTT assay. SiHa and HeLa cells were treated with different concentrations of (0, 20, 40, 80, 160 μM) of ALA for 24, 48 and 72 hrs. In SiHa, ALA reduced the viability at 160 μM concentration to 85.05±0.07% and 69.76±0.006 % at 48hrs and 72hrs respectively. In HeLa, ALA reduced viability at 160 μM concentration to 91.1± 0.1% and 67.94 ± 0.09% at 48hrs and 72hrs respectively. The data has been presented as mean ± SEM of three independent experiments. Statistical significance was assayed by one-way ANOVA. **$p<0.001$,***$p<0.0001$.
In SiHa cells ALA inhibited HDAC activity by 72.99%, 44.89% and 39.78% at 20, 40 and 80 μM concentrations. Also, on treating HeLa with different doses of ALA, it inhibited HDAC activity by 14.52%, 53.27% and 60.11% at 20, 40 and 80 μM concentrations, respectively. Data has been presented as mean ± SEM of three independent experiments. Statistical significance was assayed by one-way ANOVA***$p<0.001$

Conclusion: ALA exhibited significant inhibition of HDAC1 and DNMT1 expression in cervical cancer lines indicating epigenetic modulation in cervical cancer cells.

4.**Title:** Evaluating the potential of cinnamaldehyde loaded iron oxide nanoparticles for targeted delivery in breast cancer. (**Project ID**: CR/16/1/P)
Funding: Nil; **Duration:** September 2016-September 2020; **Sanctioned Amount:** Nil; **Investigators**: PI- Dr. Ruchika Kaul-Ghanekar; **Ph.D. Students:** Ms. Varsha Shetty; **Animal Ethical Approval No:** BVDUMC/1883/2018/002/012

Background: Breast cancer is the most common invasive cancer worldwide, impacting 2.1 million women each year. Estimated breast cancer deaths in 2018 were 627,000,which were approximately 15% of all cancer deaths among women. Despite advanced cancer therapeutics, resistance to anticancer drugs and their side effects are the major difficulties in the treatment of breast cancer. Phytopharmaceuticals are being extensively explored as adjuncts to chemotherapy because of their anticancer activity, relative safety and

biocompatibility. However, their widespread use is restricted due to their low aqueous solubility, bioavailability, poor targeting and stability. Cinnamaldehyde, the bioactive component of the culinary spice cinnamon, exhibits excellent anticancer activity, however, its hydrophobic nature limits its bioavailability. Nanotechnology offers excellent option to significantly enhance the bioavailability and targeted delivery of such hydrophobic drugs. In the present study, we synthesized and characterized CNAD (C) loaded FITC (Fi) and Folic acid (F) functionalized Fe3O4 nanoparticles (FiCF NPs) that can effectively act as a targeted drug delivery system, which can control the release and oxidation of CNAD with excellent stability and improved bioavailability for the treatment of breast cancer.

Work done: The efficacy and mechanism of action of FiCF NPs in breast cancer cell lines was evaluated. The pharmacokinetic and biodistribution studies of FiCF NPs in rat model were performed. Further, an analytical method for simultaneous determination of Cinnamaldehyde and Cinnamic acid in rat plasma was developed and validated as per USFDA guidelines.

Results:

Breast cancer cells were treated with FiCF NPs. The FiCFNPs induced time and dose-dependent decrease in the growth kinetics of MCF 7 and MDAMB 231 cells at 24-72 h. In MCF 7, FiCF NPs decreased the cell growth at 5 µg/ml concentration by 3.10 ($p<0.001$), 2.06 ($p<0.001$) and 1.64 -fold ($p <0.001$) at 24, 48 and 72 h, respectively, compared to the untreated control cells. Similarly, at 5 µg/ml concentration of FiCF NPs, MDAMB 231 cells exhibited 1.93 ($p<0.001$), 1.79 ($p<0.001$) and 1.74-fold ($p<0.001$) decrease in the cell growth at 24, 48 and 72 h, respectively, compared to the untreated control cells.

MCF 7 and MDAMB 231 cells treated with FiCF NPs showed significant fluorescence in cytoplasm with few NPs in nucleus suggesting that the nanoparticles were being successfully internalized in the cells. It shows the potential application as a targeted probe for detection of breast cancer using optical imaging.

Dose dependent increase in the uptake of NPs was observed along with higher uptake of FC NPs, folic acid functionalized FiCF NPs in both the cell lines. FCF NPs display 2.1 and 1.8-fold increase ($p\leq0.001$) compared to untargeted FiC NPs at 1.25 µg/ml concentration in MCF 7 and MDAMB 231 cells respectively. Interestingly, uptake of folic acid-conjugated (FiCF) NPs by MCF 7 cells was 1.8 times more compared with MDAMB 231 cells.

There was a significant decrease in uptake of FiCF NPs, when MCF 7 and MDAMB 231 cells were grown in the presence of an excess amount of free folic acid compared to FCF NPs without free folic acid.

We further conducted the pharmacokinetics study to evaluate CNAD bio-availability in Wistar rats. Quantitative evaluation of Cinnamaldehyde (CNAD) in rat plasma was done at the predetermined time intervals after single i.v. dose of free CNAD (10 mg/kg) and FiCF NPs at a CNAD equivalent dose of 10 mg/kg. The quantitation was done by reverse phase HPLC. The mean plasma concentration-time profiles showed that FiCF NPs

yielded higher CNAD and lower Cinnamic acid (CA) concentrations in plasma. On the contrary, free CNAD was present at less concentration in plasma and CA from free CNAD was present in higher concentration showing its rapid conversion from free CNAD throughout study period.

The tissue distribution of the free CNAD and CNAD from FiCF NPs in Wistar rats was also evaluated. FiCF NPs administration resulted in significantly lower tissue CNAD concentrations compared to free CNAD.

We developed a simple, precise, accurate and sensitive HPLC method for the simultaneous estimation of CNAD and CA in plasma. Further, validation of the method was done according to the US Food and Drug Administration (FDA) guidelines for selectivity, precision, recovery, stability and robustness.

Conclusion: The Cinnamaldehyde-loaded iron oxide nanoparticles have potential anticancer activity with targeted delivery in breast cancer.

5. **Title:** Role of Selected Phytochemicals in Regulation of Aberrant Lipid Metabolism in Prostate Cancer. (**Project ID:** CA/17/2/P)
Funding: Nil; Duration: January 2017- January 2022; Sanctioned Amount: Nil; Investigators: PI- Dr. Ruchika Kaul-Ghanekar; Ph.D. Students: Minal G. Mahajan.

Background: Prostate cancer (PCa) is the 8th most common cancer in Indian males. In the castration resistant PCa (CRPC), genes involved in lipid metabolism pathways are targeted by androgen receptors (AR). Hence, for developing therapeutic agents and repurposing of existing drugs for PCa treatment lipid metabolism is widely being studied. Silibinin is the only phytochemical reported to affect lipid metabolism in PCa. Hence, studying the phytochemicals modulating lipid metabolism and cholesterol synthesis provide a wide scope for research in PCa. Interestingly, in our earlier studies Matairesinol reduced the viability of breast cancer cell lines. Matairesinol is a plant based lignin reported to induce apoptosis and prevent tumor growth in PCa medels. Present study focuses on evaluation of effect of Matairesinol in modulating lipid metabolism in prostate cancer model.
Work done: The effect of matairesinol (MR) on viability and growth kinetics of prostate cancer cell lines was studied. Further, to evaluate the mechanism of action of (MR), mitochondrial membrane potential was determined in cells treated with the drug.

Results: We have evaluated the effect of matairesinol on growth kinetics of prostate cancer cell line (PC-3) by Trypan blue exclusion assay. The cells were treated with different concentrations (20, 40, 80 µg/ml) of matairesinol and incubated at 37℃ for 24, 48 and 72 hours. Matairesinol altered the growth kinetics of PC-3 cells in a dose-dependent manner. Moreover, at 80 µg/ml concentration, matairesinol exhibited a dose-dependent decrease in

JC-1 fluorescence intensity (Fig 3A and B, respectively) in PC-3 cells. This indicates loss of mitochondrial membrane potential after treatment with matairesinol.

Conclusion: Matairesinol has a potent anticancer activity against prostate cancer cell lines.

6. **Title:** Targeting Tumor Associated Macrophages and Neutrophils in Cancer by Cinnamaldeyde-Folate-FITC conjugated iron oxide nanoparticles (FiCF NPs) (**Project ID**: CR/17/3/P)
Funding: Nil; Duration: May 2017 to May 2021; **Sanctioned Amount**:Nil; **Investigators: PI**- Dr. Ruchika Kaul-Ghanekar; **Ph.D. Student**: Amol Rajendra Chaudhary (DBT-JRF)

Background: Breast cancer is most frequently diagnosed cancer and a second leading cause of death in women worldwide. Tumor microenvironment influences the immune cells in development and progression of breast cancer. Tumor-associated macrophages (TAM) can exert protumoral functions. Chemokines and growth factors produced by stromal and tumor cells in tumor microenvironment recruit macrophages and may influence the phenomenon of macrophage activation into pro (M2) or anti-inflammatory (M1) subtypes. Similarly, Neutrophils under influence of tumor cells may be polarized to N1 pro-inflammatory (N1) and anti-inflammatory (N2) subtypes. Many studies have reported the control of TAM and have shown that switching TAM or M2 with M1 significantly inhibited tumor progression and metastasis. Recently, it has been shown that herbal extracts can inhibit M2 polarization induced by recombinant IL-4 and IL-13 in murine macrophages. Also, the polarization of neutrophils from N2 to N1 have antitumor effect. Thus, based on such studies the present study aims at evaluating the potential of Cinnameldehyde nanoconjugate in immunomodulation by targeting macrophages and neutrophils of breast tumor microenvironment.

Work done: The effect of FiCF NPs was studied in breast cancer mouse model

Results: In FiCF NPs treated breast cancer mouse model, we found that there was a decrease in Neutrophils-to-Lymphocyte ratio.

Conclusion: Preliminary results suggest that Cinnamaldehyde Nanoconjugate (FiCF NPs) induce immunomodulatory effect in breast cancer mouse model.

7. **Title:** Evaluation of anti-cancer potential of selected phytochemicals against breast cancer stem cells (**Project ID**: CR/18/4/P)
Funding: Nil**; Duration:** October 2018 - October 2023**; Sanctioned Amount:** Nil; **Investigators:PI**- Dr. Ruchika Kaul-Ghanekar; **Ph.D. Students**: Ms. Akanksha Mahajan

Background: Breast cancer is one of the leading causes of cancer associated deaths in women worldwide. The major setback to the patient is drug resistance and recurrence due to heterogeneous mutations that occur in various cell populations or the presence of cancer stem

cells (CSCs). The cancer stem cell (CSC) hypothesis provides a hierarchical model which explains the observed heterogeneity of cancers cells within a tumor. CSCs are uniquely capable of initiating tumor formation. Majority of cells in tumors are non- tumorigenic and are marked by limited self- renewal ability, however only a small subpopulation of cancer cells has the ability to self- renew and initiate tumors. These cells are referred to as cancer stem cells (CSCs) or tumor- initiating cells. Breast cancer stem cells (BCSCs) are shown to exhibit unique growth abilities including self-renewal, differentiation potential, and resistance to most anti-cancer agents including chemo- and/or radiotherapy. All these potential properties of BCSCs contribute to the development and overall aggressiveness of breast cancer. In the present study we would screen the bioactives that target the cancer stem cells and study the underlying mechanism.

Objectives:

1. Screening of bioactives that disrupt spheroid formation in breast cancer stem cells (BCSCs)
2. To evaluate the effect of potent bioactive on down regulate of markers responsible for stemness
3. To study the effect of potent bioactive on the mechanism underlying the anticancer activity of the most potent bioactive
4. To evaluate the effect of potent bioactive on Notch signaling pathway

Work done: Literature review was done

8. **Title:** Evaluating the effect of selected bioactives on inflammasomes in breast cancer (**Project ID**: CR/19/5/P)

Funding: Nil; **Duration:** January 2019 to January 2022**; Sanctioned Amount:** Nil; **Investigators: PI**- Dr. Ruchika Kaul-Ghanekar; **Ph.D. Students**: Prajakta Biradar

Background: Breast cancer is the second leading cause of death among women worldwide and first leading cause of death among women in India. Inflammation plays a crucial role in the establishment, progression and aggressiveness of breast cancer. Recently, it has been shown that chronic inflammation in breast cancer is associated with deregulation of inflammasome complex consisting of NOD-like receptor protein 3 (NLRP3), the adaptor apoptosis-associated speck-like protein containing a caspase recruitment domain (ASC) and caspase-1. In cancer, cellular and physiological stresses cause a rapid release of pro-inflammatory cytokines (IL-1β and IL-18) which activates the inflammasome complex and contributes to tumor growth and development. Thus, the inhibition of inflammasomes or neutralization of their products (IL-1β and IL-18) could have profound effects on tumor progression in breast cancer. In the proposed study, we would be evaluating the anticancer activity of selected bioactives in breast cancer cell lines, MCF-7 and MDA-MB-231 and most

potent bioactive would be studied for their effect on inflammasome complex and in breast cancer tumor model. All this would establish the anticancer activity and therapeutic potential of the potent bioactive in the treatment of inflammasome-mediated tumor aggressiveness in breast cancer.

Objectives

1. To identify most potent bioactive against selected breast cancer cell lines
2. Evaluating the effect of the bioactive compound in regulation of inflammasome complex and its downstream signaling pathway.
3. Elucidating the mechanism of action of the bioactive in regulation of inflammasome associated markers.
4. Studying the effect of the bioactive on tumor retardation and inflammasome related markers in breast cancer mouse model.

Work done: Literature review was done

9.**Title**: Evaluating the effect of selected bioactives on cytokine and chemokine regulation in prostate cancer (**Project ID**: CR/19/6/P)

Funding: Nil; **Duration:** January 2019 to January 2022**; Sanctioned Amount:** Nil; **Investigators: PI**- Dr. Ruchika Kaul-Ghanekar; **Ph.D. Students**: Ms. Rama A. Rajadnya

Background: Prostate cancer (PCa) has been ranked as 8thmost common cancer in Indian men, with higher incidence in urban population. Current treatment strategies such as androgen deprivation therapy for PCa lead to progression of Castration resistant prostate cancer (CRPC), as a result of self sufficiency of prostate tumor cells in androgen production. Therefore, preventing the transition to CRPC and treating CRPC effectively have become critical challenges for prostate cancer management. Recent research depicts that the elevated levels of pro-inflammatory cytokines and chemokines are major mediators of the androgen receptor (AR) activation and thus play an important role in the prostate cancer development. Plant based phytocompounds or bioactives from soy, pomegranate, tomato, tea, etc. have been shown to inhibit PCa development and progression. However, very few studies are done on the cytokines and chemokines regulation in prostate cancer using bioactives. The current study aims to evaluate the role of selected bioactives on cytokine and chemokine expression in PCa.

Objectives

1. To study the effect of different bioactives on the growth kinetics of prostate cancer cell lines
2. To study the effect of the selected bioactive on the expression of pro-inflammatory and anti-inflammatory cytokines and their respective receptors in prostate cancer cell lines
3. To study the effect of the bioactive on the expression of pro-inflammatory and anti-inflammatory chemokines and their respective receptors in prostate cancer cell lines
4. To study the effect of the selected bioactive on the expression of pro-inflammatory and anti-inflammatory cytokines and chemokines in PC3 xenograft mouse model.

Work done: Literature review was done

Name of the Programme: **Obesity-Diabetes**

1. **Title:** Evaluation of the effect of Triphala on Obesity associated Cognitive impairments (**Project ID**: OB/16/1/P)
   Funding: Generated funds; **Duration:** Sept 2016-Dec 2020 **Sanctioned Amount: Rs. 0.**28 Lakhs; **Investigators:PI-** Dr. Supriya Bhalerao; **Ph.D. Students:**Shital A Giramkar (Fellowship from Sakal India Foundation, 2019); **Human Ethical Approval:** BVDUMC/IEC/80; **Animal Ethical Approval:** BVDUMC/1891/2018/002/020

Background: Obesity associated cognitive impairment is relatively unexplored area. The growing epidemic of obesity however necessitates the need to understand this association and also to explore treatment options that can prove safe and effective. The present study is planned to evaluate the effect of Triphala in obesity associated cognitive impairment using an in vitro model of fatty acid induced lipotoxicity in neuronal cells (objective 3) and cognitive impairment in obesity in rats induced with High Fat Diet (objective 4). Before these evaluations, it was thought interesting to establish association between obesity and cognition (objective 1) and to standardize the formulation under study (objective 2). During earlier years of the project, the formulation has been standardized and a pilot study was carried out as a part of objective 1.

Work done: Based on the results of the pilot study, a study to investigate the association of obesity with cognition has been initiated this year with larger sample size. With institutional ethics committee permission, healthy, young age (18–35 y) adults of normal weight (NW: BMI 18.5–24.9 kg/m^2) and obese category (OB: BMI ≥ 30.0 kg/m^2) are being recruited. Their demographic details, clinical history, anthropometric measurements, body composition (bio-impedance method) are recorded. Following this, their cognitive capacities are assessed using Addenbrooke's Cognitive Examination – ACE-III, (2012).

Simultaneously, in this year, the work to accomplish objective 3 has also been started. Pheochromocytoma cell line (PC12) was procured from NCCS. The cells are being maintained, freeze stored & subcultured in respective media. After passaging, seeding density of cells for 24 well plate has been standardized & differentiation of the cells into neuronal cells was performed using nerve growth factor. Cytotoxicity studies are ongoing using MTT assay at different time points to confirm the complete differentiation of cells.

Results: 42 individuals have been screened, of which 22 are recruited. Further recruitment of the study participants is ongoing. The in vitro experiment on differentiated cells is also going on.

2. **Title:** Predictors of Diabetes in first degree relatives of type II DM individuals: Visceral Fat and Visceral Adiposity Index (**Project ID:** OB/17/1/I)
Funding: Generated funds; **Sanctioned Amount**: Rs. 0.25 Lakhs; **Duration** : Sep 2017-Dec 2019; **Investigators: PI**: Dr. Vijay Mate, Dept. of Pharmacology, BV Medical College; **Co-Investigator**: Dr. Supriya Bhalerao; **Project Staff** : Dr. Sarika Mane; **Ethics Approval**: BVDU/MC/54

Background: The present study is planned to investigate the association of visceral fat percentage and visceral adiposity Index (VAI) with insulin resistance (marker for risk of diabetes) in the First Degree Relatives (FDRs) of diabetic patients. The participant recruitment was started in August 2018.

Work done: During last year, 21 FDRs were recruited in the study (Total recruited

individuals=80). These individuals are categorized in three age groups according to Indian Diabetic Risk Score (IDRS) questionnaire viz. 18-35 years (n = 41), 35-49 years (n = 29) and above 49 years (n =10).

The preliminary findings revealed that as age increases the fasting sugar, HOMA-IR and Visceral adiposity index increased. Visceral fat percentage showed statistically significant correlation with HOMA-IR while VAI, which is calculated parameter using waist circumference, BMI, TG and HDL did not show correlation with HOMA-IR irrespective of the age. The detailed analysis will be done after achieving the target sample size.

3. **Title**: A Pilot Study to Evaluate the Effect of Takra Basti (enema) in Sthoulya (Obesity) (**Project ID:** OB/17/2/I)

Funding: Generated funds; **Duration**: Sep 2017- Aug 2018; **Sanctioned Amount**: Rs.0.17 Lakhs; **Investigators** : **PI**: Dr. Priyadarshani A. Kadus, College of Ayurveda, BVDU; **Co-Investigator**: Dr. Supriya Bhalerao; **Project staff**: Dr. Sarika Mane; **Ethics Approval**: BVDUCOA/EC/-3482/2017-18

Background: Obesity is related to the generation of low-grade, chronic inflammation caused due to gut dysbiosis. In the present study, we evaluated effect of Takrabasti (enema of buttermilk, an Ayurveda based probiotic, processed with mixture of anti-obesity herbal drugs) in 16 obese individuals.

Results: The results of anthropometric and biochemical parameters were presented in the last year report. It was observed that Takrabasti significantly reduced the circumferential measures and skinfold thickness after the course of enema i.e. on day 16, which reverted back to baseline levels at the end of follow up period i.e. on day 45. The blood glucose levels showed gradual reduction that was statistically significant. The insulin levels increased after the course of enemas which fell down to baseline levels after 30 days.

Along with these anthropometric and biochemical investigation, the stool samples of the patients were also collected for the gut microbiome analysis at 3 time points viz. before starting the basti procedure, after completion of the procedure (day 16) and at the end of 30 days follow up period (day 45).

Gut Microbiome analysis:

Microbial composition also showed same trend i.e. increase in the bacterial diversity on day 16 which settles back to its original composition by day 45. After treatment certain changes in the composition of major phyla was observed. Phyla like Firmicutes, Proteobacteria and Deinococcus-Thermus showed increase in abundances from 16.7%, 6.7% & 0.001% to 28.5%, 13.2% & 3.8% respectively (Fig 1). Also diversity plot (Fig 2) and abundance plot (Fig 3) clearly showed emergence of genera *Geobacillus, Meoithermus, Spingomonas, Ralstonia, Stenotrophomonas* etc. just after the treatment but their they were subsided in follow up samples. Further, slight decrease in abundance of *Prevotella* was observed which was restored again in follow up samples. It is evident from Principal Component Analysis (PCoA) plot (Fig 4) that samples for day 0 and day 45 cluster together indicating similar microbial abundance and diversity.

Fig 1: Relative abundance of different bacterial phyla in stool samples at 3 different

time points

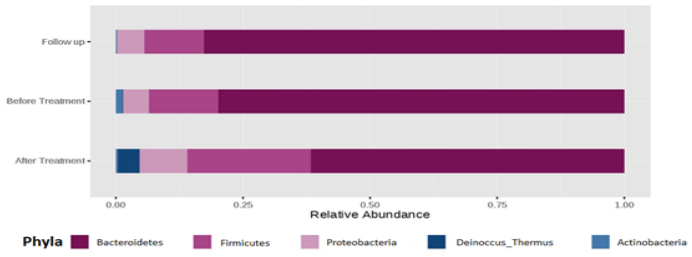


Fig 2: Relative abundance of different bacterial genera in stool samples at 3 different time points

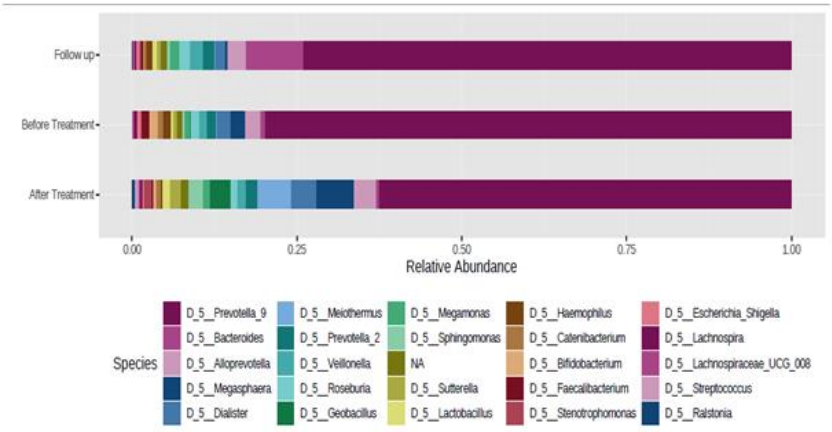


Fig 3: Plot showing abundance of different genera at different time points

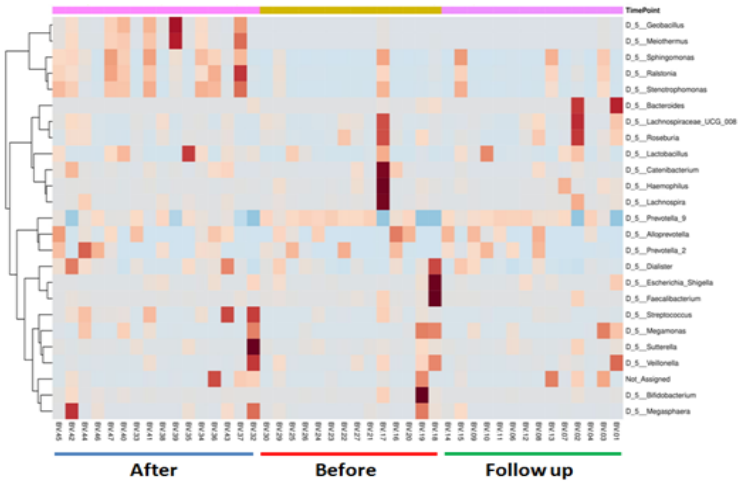
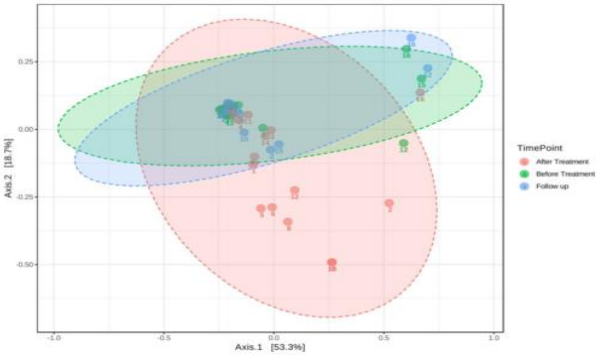


Fig 4: Beta diversity analysis. 3 distinct clusters can be observed



Conclusion: These results suggest that Takra Basti treatment is effective for a certain period of time and patients may have to undergo the same treatment repeatedly for better benefit. This effective time period can be calculated by repetitive sampling from patients after treatment. This study gives primary insights into effect of Takrabasti treatment on obese patients in physiological and microbiome perspective and also generates data for gut microbiome of obese Indian individuals.

4. **Title**:Evaluation of cardioprotective activity of an herbal formulation in rat model of isoprenaline induced myocardial infraction (**Project ID:** OB/17/1/E)
Funding:Dabur Research & Development Center, Dabur India Ltd.; **Sanctioned Amount**: Rs. 5.34 Lakhs; **EC Number**:BVDUMC/1035/2017/003/024; **Investigator**: Dr. Supriya Bhalerao; **Project staff**: Dr. Sarika Mane; **Duration**:Dec 2017- Sept 2018

Background: Isoprenaline (ISO) a beta-adrenaline agonist has been reported to produce myocardial infarction in large doses. In the present study, we investigated the cardio-protective effect of Hridyasava, a polyherbal formulation, developed by Dabur India Limited in ISO induced myocardial infarction in male Wistar rats. The study was carried out in 2 parts. In the first part, the dose of ISO was standardized (cumulative dose of 80 mg/kg). The results of this part were presented in the last year report.

Work done: This year we evaluated 3 escalating doses of Hridyasava in the standardized model (Part 2). The therapeutic dose was extrapolated from the recommended human dose. The drug was administered as a pre-treatment for a period of 28 days. There were 6 groups in the study, each having 8 animals (Table 3).

Table 3: Animal grouping for Part 2

No.	Group	Description
I	Normal control	No drug treatment and disease induction
II	Disease Control	No drug treatment and only disease induction
III	Atorvastatin (Standard Drug)	10 mg/ml/kg/day
IV	Hridyasava (low dose)	0.405 ml/kg/day
V	Hridyasava (therapeutic dose)	0.81 ml/kg/day
VI	Hridyasava (high dose)	1.62 ml/kg/day

It was observed that there was not much change in body weight after ISO administration and the weights in all groups were comparable. The heart weight was significantly more in the Disease Control group as compared to Normal Control group. Further in Group III, IV, and V heart weight was less but the difference was found to be insignificant as compared to Disease control. No statistically or clinically significant changes were seen in lipid profile. Although there were few changes in the electrical activity of the heart as revealed in ECG, statistically significant change was seen only in case of T amplitude. It was significantly lower in Disease Control as compared to Normal Control. Groups III and IV showed elevation as compared to Disease Control but was insignificant. In groups V and VI, the amplitude was less as compared to Disease Control but the decrease was again insignificant. In case of histopathological changes, the Disease Control group showed myocardial injury as compared to Normal Control group. Atorvastatin (standard drug) showed reduction in this injury. However, Hridyasava treated groups did not show any such reduction.

Since no dose response was observed in this part, as an extension of the project we evaluated effect of Hridyasava in fixed dose of 1 ml when administered for 14 days. For this part of the study (Part 3), the animals were divided into following 4 groups each with 6 animals (Table 4).

Table 4: Animal grouping for Part 3

No.	Group	Description
1	Normal control	No drug treatment and disease induction
2	Disease Control	No drug treatment and only disease induction
3	Atorvastatin (Standard Drug)	10 mg/ml/kg/day
4	Hridyasava	1 ml/day

Similar to Part 2, the body weights remained comparable in all groups. The heart weight was higher in Disease Control group but the difference with Normal Control was not significant. The heart weights in Groups III and IV were comparable with Disease Control. The changes observed in lipid profile were statistically or clinically insignificant.
In this part, we also evaluated the effect of Hridyasava on oxidative stress (MDA) and cardiotoxicity markers (cardiotroponin and LDH). MDA levels were significantly higher in Disease Control as compared to Normal Control (Table 5). In groups III and IV, these levels were found significantly lower as compared to Disease control.

Table 5: Effect on Serum MDA levels

Groups	Units (µM)
Group I	19.95±3.97
Group II	$51.74\pm11.27^{***}$
Group III	$30.90\pm6.51^{\#\#\#}$

Group IV	36.86±5.42[#]

Values expressed as Mean ± SD, ***p< 0.001 as compared to Group I, [#] p<0.05; [###] p<0.001 as compared to Group II

Cardiotroponin levels did not show significant changes while LDH levels were higher in Disease Control group as compared to Normal Control group. In groups III and IV, these levels were low but the difference was insignificant as compared to Disease Control (Table 6).

Table 6: Effect on serum LDH levels

Groups	**LDH(nmol/min/mL)**
Group I	737.30±257
Group II	971.62±159***
Group III	740±289[###]
Group IV	770.06±93.30[#]

LDH values expressed as Mean ± SD
***p< 0.001 as compared to Group I, [#] p<0.05; [###] p<0.001 as compared to Group II

Effect of Hridyasava on electrical activity of heart:
As compared to Normal Control, PR interval was lower in Disease Control group, while the parameters like QRS interval, QT interval, T peak, JT interval and P duration weresignificantly higher. In groups III and group IV, these parameters were not affected muchand appeared comparable to Disease Control. Similarly, parameters like RR interval, Heart rate, ST height appeared comparable in all groups (Table 7).

Table7: Effect of Hridyasava on electrical activity of heart

Parameters	**Group I**	**Group II**	**Group III**	**Group IV**
RR interval (s)	0.16±0.02	0.17±0.03	0.18±0.06	0.16±0.01
Heart Rate (BPM)	392.63±46.88	359.98±55.21	364.55±80.02	378.96±28.77
PR interval (s)	0.05±0.005`	0.043±0.003*	0.042±0.004	0.043±0.003
QRS interval	0.0218±0.0033	0.0174±0.0011**	0.0167±0.0021	0.0177±0.0011
QT interval	0.065±0.008	0.081±0.009**	0.084±0.009	0.075±0.005
ST height	0.003±0.063	0.072±0.038	0.072±0.048	0.062±0.037
S amplitude	-0.12±0.106	0.031±0.043*	0.022±0.05	0.014±0.104
T peak tend interval	0.031±0.009	0.042±0.006*	0.043±0.008	0.037±0.003
JT interval	0.043±0.011	0.063±0.009*	0.068±0.011	0.058±0.005
QTC	0.17±0.03	0.20±0.03	0.21±0.03	0.19±0.02

P duration(s)	0.0197±0.0024	0.0168±0.0005*	0.0167±0.0025	0.0187±0.0009
T amplitude	0.168±0.07	0.19±0.034*	0.239±0.075	0.209±0.038

Conclusion: Based on our findings we can conclude that Hridyasava has potential which need to be confirmed using high dose of drug administered for longer duration. The formulation can be further tested using cardiomyocytes (in vitro model).

5. **Title**: Effect of Nishamlaki in patients with Polycystic Ovarian Syndrome (Project ID: OB/17/2/E)
Funding: Pharmanza Herbals Pvt. Ltd.; **Duration** : July 2017- Jan 2019; **Sanctioned Amount**: Rs. 5. 45 Lakhs; **Investigator (s)**: **PI :** Dr. Vijaya Pandit, Dept. of Pharmacology, BV Medical College; **Co-Investigator**: ;Dr. Supriya Bhalerao; **Project Staff**: Dr. Poonam Gupte; Dr. Shubhangi Harke; **Ethics Approval** : BVDU/MC/E36

Background: Nisha- Amalaki (NA) a polyherbal formulation is widely used in the treatment of diabetes. As Polycystic Ovarian Syndrome (PCOS) is associated with insulin resistance, it was thought interesting to evaluate the effect of NA in patients with PCOS. A randomized, prospective clinical study was carried out and the effect of NA was assessed as on clinical, biochemical, hormonal and radiological parameters.

Work done: Total 51 patients were screened for the study of which 48 patients gave informed consent and were recruited in the study. Out of the total patients recruited, 21 patients completed the study. The recruited patients were allocated into three groups Nishamlaki (NA), Metformin (M), Nishamlaki and Metformin combination (NA+M).

Results: Out of the total 21 participants recruited in the study, six were allocated to NA, eight were treated with metformin alone, and seven participants were treated with a combination of NA and Metformin (NA+M). The baseline characteristics of PCOS of the participants are described in Table 1.

Table 1: Baseline characteristics of the recruited patients

Group	NA	M	NA + M	p value
No. of participants	6	8	7	-
BMI (kg/m2)	23.38 ± 4.11	22.87 ± 5.04	29.67 ± 7.6	0.0756
Irregular menses(n)	6 (100%)	8 (100%)	7 (100%)	-
Hirsutism (n)	1 (16.7%)	1 (12.5%)	2 (28.6)	-

Effect of treatment on various study parameters:
In all the treated groups, HOMA-IR decreased significantly. The mean endocrine profile (FSH, LH, LH/ FSH and testosterone) was found to be unaltered irrespective of the treatment. The mean total cholesterol was found to be significantly decreased in females treated with metformin alone. The other parameters of lipid profile (TG, HDL, and LDL) were found to

be unaltered in all the treated groups. Mean ovarian volume was found to be significantly decreased in PCOS females treated with NA and NA in combination with metformin.

Conclusion: Insulin resistance is hallmark observed in PCOS condition. Treatment with NA, metformin and combination of NA+ metformin was beneficial in decreasing insulin resistance in PCOS patients after three months duration. Mean ovarian volume was found to be decreased by NA and also in group receiving combination of NA with metformin. Though the study was conducted in a small number of patients and for short duration, Nishamlaki was seen to be as effective as Metformin in the treatment of PCOS condition

Table 2: Effect of treatment on various biochemical parameters
Values expressed as Mean± SD, *p<0.05 compared to before treatment value

Parameters	**Nisha-Amalaki (NA)**		**Metformin**		**NA+ Metformin**	
	Before	After	Before	After	Before	After
HOMA-IR	2.42 ± 2.07	1.60 ± 1.67*	2.21 ± 1.04	1.54 ± 0.88*	3.18 ± 1.99	2.34 ± 1.86*
FSH (IU/ml)	5.03 ± 0.91	5.71 ± 1.33	5.40 ± 1.17	6.49 ± 1.76	5.24 ± 2.12	5.65 ± 1.74
LH (IU/ml)	9.88 ± 8	6.86 ± 3.8	6.92 ± 2.91	6.93 ± 2.52	7.84 ± 7.04	5.19 ± 2.27
LH/FSH	2 ± 1.52	1.53 ± 0.63	1.23 ± 0.52	1.19 ± 0.48	1.57 ± 1.39	0.94 ± 0.34
Free Testosterone (pg/ml)	3.83 ± 1.74	3.02 ± 1.27	3.15 ± 1.21	2.85 ± 1.47	4.21 ± 3.51	6.89 ± 7.52
TC (mg/dl)	183.33±47.5	165.67±46.6	173.63±33.41	160.75±27.08*	172.14±21.28	161.14±28.24
HDL (mg/dl)	49.33 ± 7.17	48 ± 9.57	45.88 ± 14.03	41.38 ± 8.55	47.89 ± 10.74	43.86 ± 7.96
TG (mg/dl)	91.67 ± 36.9	92 ± 43.07	112 ± 51.67	103.5 ± 35.65	88.86 ± 29.77	88.71 ± 31.29
LDL (mg/dl)	108.17 ± 39.4	97.17 ± 29.7	96.5 ± 18.6	97.13 ± 24.4	103.71 ± 21.83	96.51 ± 23.58
VLDL (mg/dl)	18.31 ± 7.4	18.32 ± 8.7	22.41 ± 10.36	20.71 ± 7.88	17.78 ± 5.96	17.81 ± 6.36
Mean ovarian volume (cc)	10.53 ± 1.88	8.50 ± 1.84*	11.64 ± 3.60	10.51 ± 3.89	14.34 ± 6.37	13.72 ± 6.24*

6. **Title**:Association between Prakriti (Ayurvedic concept of constitution) and presence of Metabolic Syndrome (**Project ID:** OB/17/3/I)
Funding: Generated funds; **Sanctioned Amount**: Rs.0.18 Lakhs; **Investigators**: **PI** : Dr. Supriya Bhalerao; **Co-Investigator** : Dr. Jayshree Gothankar, Dept. of Community Medicine, BV Medical College; **Project staff**: Dr. Poonam Gupte; **Duration**: Jan 2017 - Dec 2019; **Ethics Approval**: BVDUMC/IEC/95A

Background: Prakriti of an individual is defined by the relative proportions of the three doshas (functional entities in the Ayurvedic paradigm) Vata, Pitta and Kapha. These three entities represent distinct characteristics and therefore body functions. The dominant functional entity determines the phenotype. The phenotype of a person is identified based on appearance, temperament and habits of an individual and this phenotype is described to be responsible for susceptibility of the person to specific disease. With this background, we planned the present study to explore the association of Prakriti with presence of Metabolic Syndrome (MS). MS is a cluster of at least 3 of 5 medical conditions viz. large waist size, elevated blood pressure, fasting blood glucose & triglycerides and low levels of high density cholesterol.

Results: During last year, 15 individuals were recruited (Total recruited 82). Of the 82 individuals, 32 are males and 50 are females. Screening and recruitment of the participants is still ongoing so as to complete target sample size of 100 individuals. Out of total screened individuals, 29 individuals had IDRS $\geq$ 60. The majority of individuals had pitta prakriti.

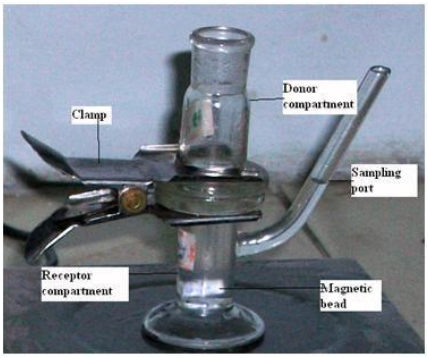
7. **Title:**Comparative study of different processing methods on Barley (Yava), an indigenous cereal for its effective use in metabolic diseases (**Project ID: OB/18/3/E**)
Funding: Indian Association for the Study of Traditional Asian Medicine; (IASTAM-India) student fellowship; **Duration:** October 2018-July 2019; **Sanctioned Amount: Rs.0.**50 Lakhs; **Investigators: PI-:**Shital A Giramkar; **Human Ethical Approval:** BVDUMC/IEC/80; **Animal Ethical Approval:** BVDUMC/1891/2018/002/020

Background: Barley (Yava) is an ancient indigenous cereal reported in Ayurvedic literature to be used in metabolic diseases like obesity and diabetes. This claim in Ayurveda has also been validated using in vitro, in vivo and clinical studies. In spite of having substantial therapeutic potential, it is not commonly consumed as its relative counterparts like oats in the Indian diet though few products of barley are available in the market. There issues like public perception as non- food grain, low functional gluten, poor palatability (as hull contains tannic acid which gives a bitter taste) and high ash and raw fiber content which restricts its use as a food grain. Interestingly, Ayurveda describes various processing methods to convert barley in palatable form like pearling, dry roasting, roasting with ghee, fermenting, soaking in herbal decoction/s followed by drying etc. There are no scientific studies available on these methods to ascertain whether these methods actually overcome the drawbacks listed above and at the same time

maintain/improve the therapeutic potential of the barley.

Work done: In the present project, barley flour was processed by 3 different methods viz. roasting, roasting with ghee and soaking in Triphala decoction. All these processed varieties were analyzed using different parameters such as proximate composition, biological activity (anti-oxidant and anti-glycation potential), β- glucan estimation followed by permeability study (Fig.5: Franz cell diffusion) and were compared with each other as well as with the unprocessed barley flour. All three processed forms showed variation in physicochemical & biochemical parameters.

Fig. 5: Franz cell diffusion Assembly



Results: Proximate analysis of all four processed Yava showed variation and inconsistency for all processed methods (Table:1). The anti-glycation activity was found improved in all 3 processed forms though the one processed with Triphala decoction showed the best activity. The anti-oxidant activity did not show much alteration due to any of the processing methods. β-glucan concentration was high in roasted yava (6.22%). The permeability of the soluble fiber was found approximately 42%, 54%, 28% & 32% in plain barley, roasted, roasted with ghee & soaking in Triphala decoction respectively. As mentioned above roasting has shown higher % soluble fiber after diffusion assay which can be correlated with higher content of β-glucan extraction.

Table 8: Comparison of plain and processed forms of barley in terms of various studied parameters

Parameters (%)	**Plain Barley**	**Roasted barley**	**Roasted with ghee barley**	**Soaked in Triphala decoction barley**
Proximate analysis				
Moisture content	6.2 ± 0.5	6.05±0.1	5.9±2.5	7.3±0.4
Ash value	3.3 ± 0.28	3.8±0.0	3.7±0.1	6.9±0.2
Crude fat	4.9	4.4	8.5	4.0
Carbohydrate	64.07±2.3	59.72±1	54.11±2.9	51.6±2.5
Insoluble fiber	16.74±0.06	19.38±0.02	23.89±0.1	26.74±0.06

Soluble fiber	7.06±0.02	4.61±0.01	6.00±0.04	6.2±0.02
Biological Activity				
Anti-oxidant activity				
Total Phenol Content	13±1.5	12.17±2.47	10.17±0.76	34.77±0.75
ABTS radical scavenging activity	22.95±1.2	21.35±0.49	20±0.71	19.35±0.21
Anti-glycation activity *				
Fructosamine Inhibition	10.62 ± 0	14.46 ± 2.	19.27 ± 9.5	15.42 ± 6.80
Protein Carbonyls Inhibition	34.62 ± 3.89	7 82.42 ± 1.55	43.96 ± 4.66	60.44 ± 1.55
Protein amyloids Inhibition	39.66 ± 4.87	43.97 ± 8.53	43.10 ± 2.4	69.83 ± 1.21
β-glucan estimation	3.94± 0.93	6.22± 0.79	3.66± 0.68	4.95± 0.39
Permeability of soluble fiber content	42	54	28	32

(* % inhibition as compared to positive control)

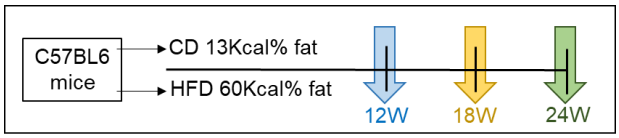
Conclusion: From the preliminary findings, roasted barley appears to be the best form. These findings however need to be confirmed.

8.Title of the project: Regulation of hematopoietic stem cell function in obesity by mitochondrial metabolism. (Project ID: OB/18/4/E)
Funding: DBT-Wellcome India Alliance; **Duration:** Sept 2018-Aug 2023; **Sanctioned Amount:** Rs. 3.43 crores
Investigators: PI- Dr. Ashwini S. Hinge; **Research Technician:** Mr. Chetan Chavan; **Animal Ethical Approval**: BVDUMC/1886/2018/002/015 and IAEC/2018/B-349

Background: Hematopoietic stem cells (HSCs) have inherent property of self-renewal and differentiation. These properties are crucial to maintain finite stem cell pool and for sustained hematopoiesis. The regulatory mechanisms defining stem cell fate decision – whether to self-renew to preserve stemness or commit to differentiation to produce myeloid and lymphoid lineages are of utmost importance but still remain elusive.
HSCs depend on metabolic cues to maintain its different cellular stages like quiescence, cell activation and stepwise differentiation. During this, HSCs switch from glycolysis to oxidative phosphorylation for energy production which is provided by mitochondria. How metabolic cues in HSCs regulate its function and maintain balanced fate decisions is still not well understood. Hence, understanding these metabolic cues are utmost important to improve hematological outcome especially in stress hematopoiesis and diseased conditions. Understanding these mechanisms are crucial to develop effective protocols for effective bone marrow transplantation and for the treatment of hematological disorders.

Obesity is a complex patho-physiological condition causing metabolic disruption and also leads to compromised HSC function. However, how mitochondrial metabolism plays role in modulating HSC function in obesity is still not known. Hence, we hypothesize that obesity condition alters mitochondrial metabolism further altering HSC function.

Work done:
[1] Establishment of mouse model: Schema of diet induced obesity mouse model:



Diet induced obesity mouse model was used for the study. C57BL/6 mice (male and female) were fed ad libitum on commercially available control diet; CD (13Kcal% fat) and high fat diet; HFD (60Kcal% fat) for 12 to 24 weeks. All animal experiments were approved by institutional ethical committee. Mice were weighed every week to monitor changes in whole body weight of each mouse. Mice will be sacrificed after 12, 18 and 24 weeks of feeding and bone marrow (BM) cells will be used for analyses of various parameters.

[2] Analyses of hematopoietic stem cell progenitors (HSCP) frequency:
Isolated BM cells were immuno-stained for cell surface markers specific for long-term HSCs (LT-HSCs), short-term HSCs (ST-HSCs), for progenitors and for myeloid and lymphoid lineages. The immuno-stained cells were analyzed by flow cytometry.

[3] Analyses of mitochondrial function: Specific mitotracker dyes were used to detect various mitochondrial parameters. Mitotracker green FM detects mitochondrial mass in active mitochondria only, tetramethylrhodamine-ethyl ester (TMRE) measures mitochondrial membrane potential; MMP and mitoSOX redR detects mitochondrial reactive oxygen species; mROS and DCFDA for overall ROS were used. These parameters were analyzed in HSCPs by flow cytometry.

Results and Conclusion:
[1] Assessment of whole body weight: As expected, we observed that at 12 weeks, mice fed on HFD showed significant increase in body weight as compared to mice fed on CD.

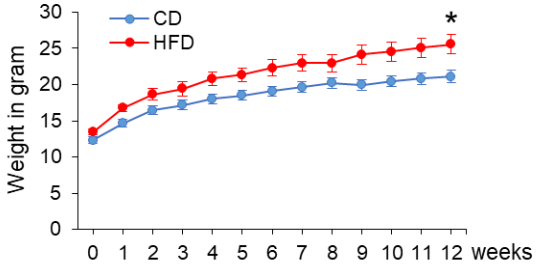


Figure 1: Kinetics of weight gain in CD and HFD fed mice. At 12 weeks mice fed with HFD showed significant increase in weight as compared to CD fed mice (n= 9-10 mice/group).

[2] Hematopoietic stem and progenitor pool is similar between CD and HFD mice:
Frequency of LT-HSCs (lin$^-$Sca$^-$1+c-Kit$^+$CD150$^+$CD48$^-$CD34$^-$), short-term HSCs (lin$^-$Sca$^-$1+c-Kit$^+$CD150$^+$CD48$^-$CD34$^+$), SLAM ((lin$^-$Sca-1$^+$c-Kit$^+$CD150$^+$CD48$^-$), LSK (lin$^-$Sca-1$^+$c-Kit$^+$) and LK (lin$^-$c-Kit$^+$) was similar between the groups. Progenitor cell population – Megakaryocyte-Erythrocyte progenitor (MEP), Common Myeloid Progenitor (CMP) and Granulocyte Macrophage Progenitors (GMP) remain unchanged between the groups. Myeloid and lymphoid lineage reconstitution of the groups was comparable. Thus, our preliminary data suggest short-term exposure to HFD did not affect stem and progenitor pool in mice. We will be assessing whether HSCs rom both these groups are functional by performing serial transplantation experiments.

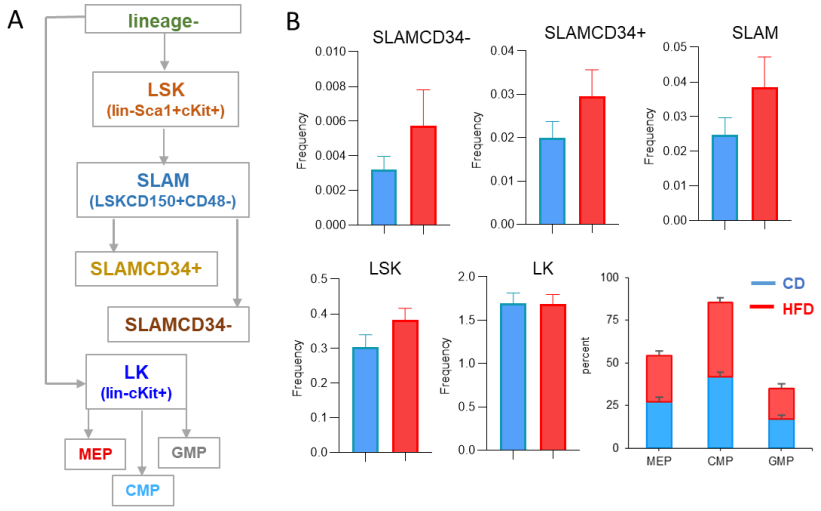


Figure 2: [A] Schema of gating strategy for hematopoietic stem cell and progenitor population. [B] Analysis of HSCP frequency. Whole bone marrow cells isolated from CD and HFD fed mice were immuno-stained for defined specific cell surface markers identifying HSCPs (n = 9-10 mice/group, avg ± SD).

[3] Analyses of mitochondrial function:
Since obesity induces oxidative stress, firstly we analyzed overall ROS production in LSK-SLAM cell population. There was no change in overall ROS production in LSK-SLAM cell population of HFD fed mice versus CD fed mice. Importantly, mROS was increased in HFD compared to CD groups in LSK-SLAM cell population. MMP was marginally high in HFD group. As expected, active mitochondrial mass remained unchanged between the groups. Taken together, the preliminary data indicate that short-term exposure to HFD led to increase in mROS and MMP levels suggesting alteration in mitochondrial function/ health.

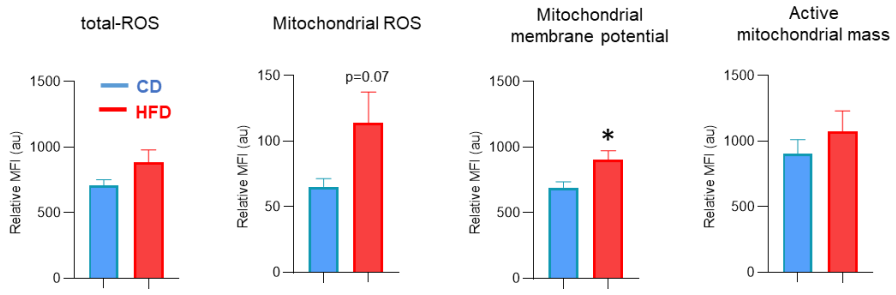


Figure 3: Analysis of mitochondrial parameters in LSK-SLAM population. Whole bone marrow cells isolated from CD and HFD fed mice were immuno-stained for cell surface markers for LSK-SLAM followed by mitotracker dyes to measure specific mitochondrial parameters (n = 9-10 mice/group, avg ± SD).

9. Title : Effect of Yoga intervention on skeletal muscle linked glucose homeostasis in pre-diabetic individuals (**Project ID:** OB/19/5/E)
Funding: DST (SATYAM); **Duration**: March 2019-March 2022; **Sanctioned Amount** : Rs.46. 74 Lakhs; **Investigators**: **PI** **:** Dr. Supriya Bhalerao; **Co-Investigator (s)**: Dr. Jayshree Kharache; Mrs. Anita Patil; **Project Staff**: Dr. Tanuja Sawant (SRF); Dr. Shubhangi Harke (JRF); **Ethics Approval**: IEC/2019/05

Background: Currently diabetes prevalence is rising in India. India ranks second in case of pre-diabetes a non-symptomatic condition which occurs before manifestation of overt diabetes. It is imperative to identify the individuals in pre-diabetic state and prevent/delay their progression to diabetes through proper interventional strategies like physical exercises.

In the present study, pre-diabetic individuals will be treated with Yoga or exercise for a period of 4 months. The effect of these interventions will be assessed on muscle function and strength since skeletal muscles are major site for glucose disposal and their strengthening may enhance proper glucose disposal. It is expected that the project will enable to bridge the gap in existing knowledge about Yoga and its effect on skeletal muscle linked glucose homeostasis. To understand this the objectives of the present study are i) To evaluate the effect of Yoga interventions on muscle mass, strength, endurance and flexibility which are direct or indirect indicators of fat deposition in skeletal muscles & ii) To study the association between changes in muscle quality/ functionality and glycemic control.

Work done: The study documents (Case record form, Patient information sheet, Informed consent form) and study information material (banners, posters and pamphlets) have been prepared. The Institutional Human Ethics Committee permission to conduct the study has been sought. The campaign to propagate the information about the project is being carried out on Bharati Vidyapeeth campus. The individuals who meet the necessary criteria of the study are being screened. Total 10 individuals have been screened so far for detection of pre-diabetes. Their blood investigations (Fasting blood glucose and HbA1c) have been carried out.

1.**Title:** Studies on Vidanga-Traditionally used plants with respect to their Pharmacological Activities (**Project ID**: HM/18/1/P)
Funding Agency: NA; **Duration:** Registered August (2018); **PhD Student**: Kartikey T Jagtap; **Name of the Guide**: Dr. Suresh D. Jagtap
Background: Vidangahas several medicinal properties. Different species are correlated with local name Vidangathroughout India and investigated for their medicinal properties. Vidanga is one of the herbs commonly used in Ayruveda. It is considered to support the intestine and keep the digestive system healthy. The genus Embelia belongs to family Myrsinaceae. Species of Embelia like E. ribes, E. basaal, E. **drupacea** and Maesaindica are known for their medicinal use since thousands of years.Vidanga has strong traditional as well as experimental base for its use: in skin ailments like acne and pimple; in constipation; digestive track in piles; as a brain tonic. Therefore parameters related to these conditions will be studied to find out potent Embeliaspecies as Vidanga.
The market samples of Vidanga are available in mixtures of aliedVidanga species, so we can observe ambiguity in the market drugs

Objectives:

- To identify and collect all Vidanga species and development of simple field identification ke To study the ambiguity in identification of authentic Vidanga drugs from market samples using In-vitro comparative antioxidant studyTo study more effective species of Vidanga using In-vitro comparative antioxidant study on self-collected samples
- To carry out pharmacogonistic studies on fruits of selected Vidanga species using In-vivo anti-inflammatory studies
- To confirm the most potent species of Vidanga by pharmacogonistic studies using In-vivo immunomodulatory potential

2.**Title:** Chemometric analysis & Development of Methodology for quality standardization of 'Vidanga' (**Project ID**: HM/18/2/P)
Funding Agency: CSIR HRDG JRF; **Duration:** January 2019 - March 2023; **PhD Student**: Manoj Khavate; **Name of the Guide:** Dr. Suresh D. Jagtap

Background: Therapeutic properties of the genus Embelia are attributed by Embelin or embolic acid present in berries of plants, The concentration of active principle in plants may varyon account of environmental conditions or ecosystem of the plant, maturity at the time of collection, substitutability on the basis of perceived efficacy or generic name and adulteration are obvious. These factors cause ambiguity for authentication of Embelin in the traded herbal raw materials; therefore there is a need to standardize a method for rapid, accurate and non-destructive method to detect the authentic species.

Objectives: Development of standardization parameters by co-relating biological activity and chemometric parameters Generation of biological activity based chemical profile of Vidanga

1. The Chemometric standardization of Vidanga will throw light on rapid, non destructive detection method for authentic species.

2. The study can set a model to solve problem related to ambiguity among the traditionally used plants.

Name of the Programme: Communicable Diseases

1.**Title:** Establishment of a novel Electronic Surveillance System for dengue in Pune: an initiative for Smart Cities Mission **(Project ID**: CD/18/1/E)
Funding: ICMR; **Duration:** March 2017 – February 2020; **Sanctioned Amount**: Rs. 400.1 Lakhs; **Investigators: PI** - Dr A. C. Mishra; **Co-Investigators** - Dr Vidya Arankalle (IRSHA), Dr Sanjay Lalwani, Dr Arundhati G Diwan, Dr. M Modak (Bharati Vidyapeeth Medical College), Anand P Kulkarni, Dr Varsha Vaidya; **Ph.D. Students**: None; Human Ethical Approval: IEC/2017/04, renewed IEC/2018/11

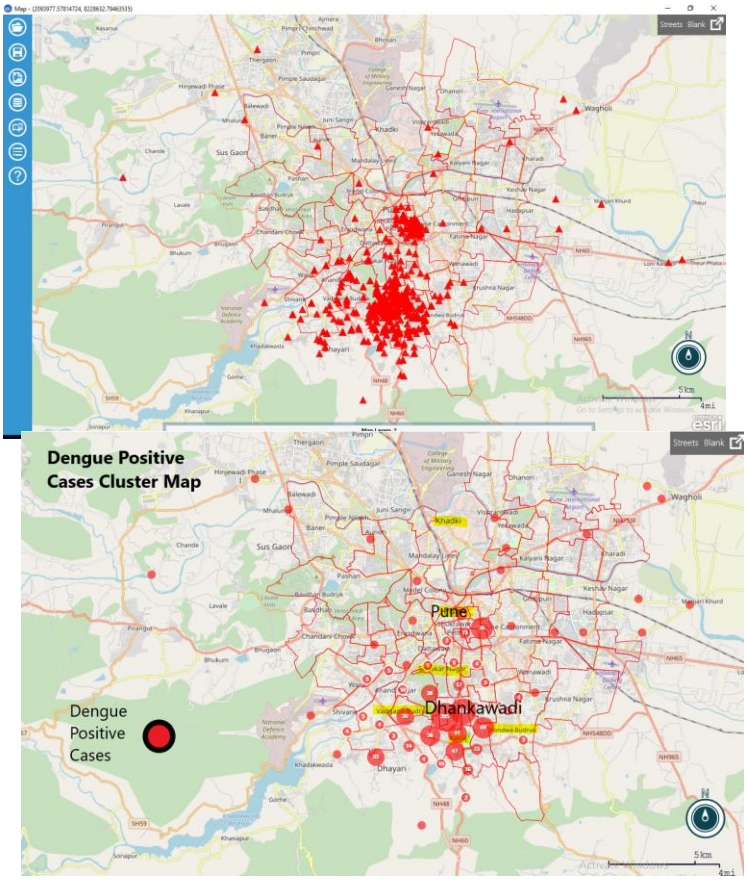
Work done: Development of web-based electronic system to collect, store, retrieve and process data As proposed to develop a secure, sensitive and robust electronic system for collection, storage, analysis and streaming of results, we utilized CDC.Epi-info software program. Epi Info is a public domain software package designed for the global public health community practitioners and researchers by CDC, USA. We have customized the software as per our requirement and able to record following features:
Demographic Information:- This page consists of personal information like name, age, sex, address, etc.
Clinical Information:- Sign and symptoms of the patient along with parameters like pulse, blood pressure, tourniquet test and hematological tests (Only for IPD patients) are included here.
Socio-economic status:- Information related to educational, economical and habitat is to be filled in this page.
Other benefit of using this software includes:
Easy access to questionnaire and database construction, data entry and analysis with epidemiologic statistics, graphs, and maps.
Demographic and clinical information could be collected in the field directly on tablet / mobile and transmitted real-time to central server both online as well as by connecting the mobile with computer.
Laboratory results are entered into system online. Different test result template can be generated through the algorithm in the software.

Real time monitoring of data
We created dashboard to get automatic results on daily basis. The positive and negative cases were plotted as spot or cluster on Pune map (Figure 1). Seasonal trend, age and sex-wise distribution get upgraded automatically after new entries. Dashboard data could be successfully shared with stakeholders like clinicians, laboratory and data collectors on real time basis. On enlargement of maps, we can pinpoint actual cases with location details on the map for any intervention.

Figure 1: (A) Spot and (B) Cluster map of positive cases, updated daily on dashboard

(A)

(B)



Clinical spectrum of dengue during 2018 season

Dengue surveillance was continued in Dhankawadi ward. The ward included one corporation hospital (Pote hospital), tertiary care hospital (Bharati hospital) and two clinics of general practitioners (GP). In view of the importance of pediatric dengue, we included one pediatric hospital (Mankar Hospital) from different ward (Sinhgad Road). Figure 2 depicts the distribution of suspected cases and confirmed (positive for NS1 and/or IgM-anti-DENV antibodies in ELISA) dengue cases during the July 2018 - June 2019. The month of October witnessed peak for confirmed dengue cases.

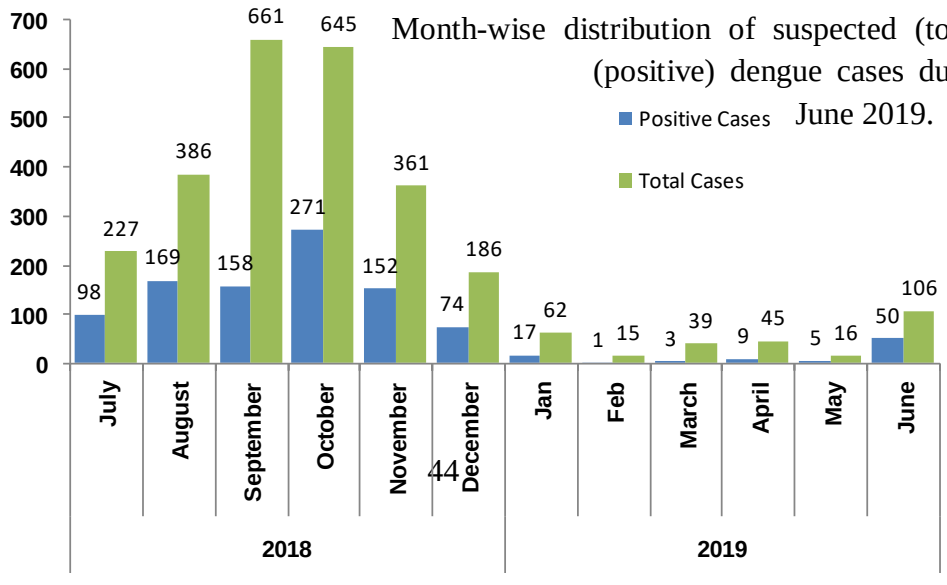


Figure 2: Month-wise distribution of suspected (total) and confirmed (positive) dengue cases during the July 2018 - June 2019.

A total of 2748 samples were collected from dengue suspected patients. All samples were tested for NS1 antigen and anti-DENV IgM antibody using J Mitra NS1 ELISA and Panbio Dengue IgM Capture ELISA respectively. A total of 1002 (36.5%) showed the presence of NS1 and/or IgM markers and were confirmed to be positive for DENV infection. Of these, 323 (32.2%), 280 (27.9%) and 399 (39.8%) were found to be positive for NS1, IgM and dual NS1/IgM positive respectively. Of these, 960 were tested for anti-DENV IgG using Panbio Capture ELISA and 353 (36.8%) were found to be positive for secondary dengue infection.

To determine the circulating serotypes, a total of 99 NS1 positive serum samples were tested for CprM
based diagnostic RT-PCR. We successfully PCR amplified 57 out of 99 (57.6%) dengue confirmed
samples. NS1 RT-PCR based method was used for serotyping. Serotype distribution for 51 positive
samples revealed presence of DENV-1 in 15 (29%), DENV-2 in 2 (3.9%), DENV-3 in 29 (56.7%) and
DENV-4 in 2 patients (3.9%). DENV-3 serotypes were found to be predominant during 2018 dengue
season. Additionally, co-infection was detected in 3 patients (5.8%), one each with serotype DENV-1/-2,
DENV-1/-3 and DENV-2/-3.

95 NS1 positive serum samples were used to isolate DENV by infecting Vero cells. 52 (54.7%) DENV isolates were obtained of which 47 were serotyped as DENV-1 – 16 (30.7%), DENV-2 – 04 (7.7%) and DENV-3 – 27 (51.9%).

2.**Title**: Immune response of Indian preterm infants to pentavalent vaccine (**Project ID**: CD/18/2/E)
Funding: DHR-ICMR; **Duration**: July 2017 – June 2019; **Sanctioned Amount**: Rs.34.22 Lakhs
Investigators: PI - Dr Vidya Arankalle; **Co-Investigators** - Dr A. C. Mishra (IRSHA), Dr. Nandini Malshe, Dr Sonali Palkar, Dr Sanjay Lalwani (Bharati Vidyapeeth Medical College); **Human Ethical Approval**: IEC/2017/31

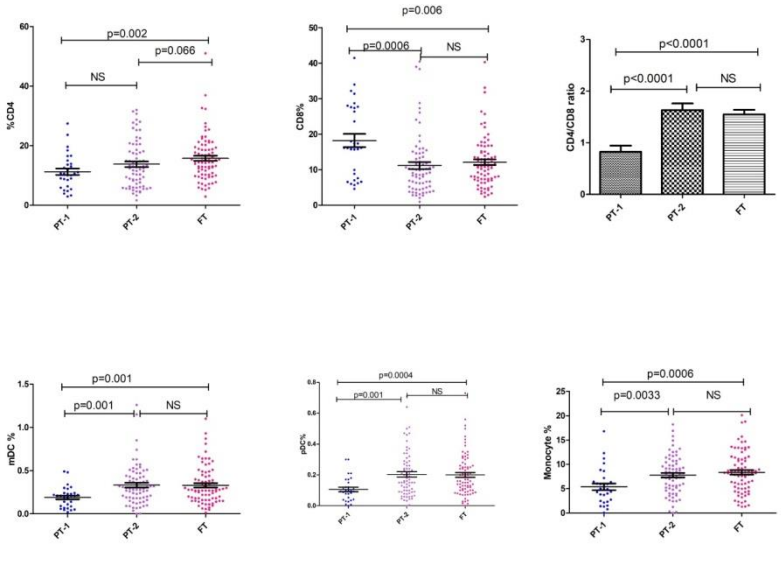
Work done: In the year 2018-2019, the enrolment number of infants reached 194. These included: 80 infants born full term (FT) and 114 born preterm (PT). Of these, 34 were born during 28 -32 week of gestation (PT-1) and 80 were born during 32 -36 week of gestation (PT-2). Follow up samples were collected from 136 babies approximately 1month after the third dose of the pentavalent vaccine (FT = 54, PT-1 = 24 & PT-2 = 58). On receipt of the blood samples at enrolment or at follow up, whole blood is subjected to flow cytometry for the quantitation of immune cells.

Prior to pentavalent vaccination, preterm infants showed lower frequency of CD4 cells (PT-1, 10.6%; PT2, 12.55%) when compared to FT infants (14.4%, p=0.002 and 0.06 respectively). The proportion of CD8 T cells was higher in PT-2 (16.2%) than in PT-1 (9.13%; p=0.0006) and FT (10.9%; p=0.006) infants (Figure 3A). In addition, subsets of dendritic cells, showed significantly lower percentages of mDC-0.21%; pDC-0.094% in PT-1 as compared to PT-2 [(mDC-0.29%; p=0.003) & (pDC-0.16% p=0.006)] and FT infants [(mDC-0.27%; p=0.001) & (pDC-0.16%; p=0.0001)]. Frequency of monocytes in PT-1 infants (4.88%) was considerably low as compared to PT-2 (7.8%; p=0.002) and FT (8.18% p=0.001) infants.

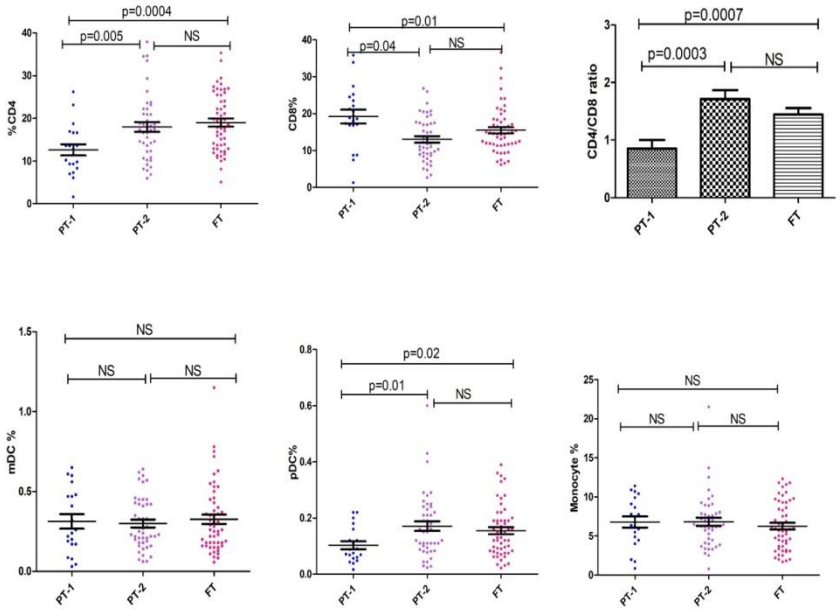
Post pentavalent vaccination during follow-up visit, similar trend of lower frequency of CD4 and higher CD8 cells was observed in PT-1 as compared to PT-2 and FT infants. Frequencies of monocytes and mDCs were comparable among the study groups but frequency of pDCs was still less in PT-1 as compared to PT-2 and FT infants (Figure 3B).

Figure 3: Quantitation of major immune cells and comparison among all study groups at enrolment visit i.e. pre-vaccination (A) and at follow-up visit i.e. one month after vaccination (B). Error bars indicates Mean ± SEM

(A)



(B)



Antibody titers against pentavalent vaccine components:

Plasma IgG titres measured before vaccination reflect maternal transfer of antibodies. At enrolment, IgG titres of anti-Ttx (tetanus toxoid), anti-PT (Bordetella) and anti-Hib (Haemophilus influenzae B) were higher in FT infants as compared to PT infants, whereas anti-HBs and anti-Dtx (diphtheria toxoid) IgG were comparable among the groups. (Figure 4.1). Post vaccination, plasma IgG titres of anti-Ttx, anti-Hib and anti-HBs were higher in FT infants as compared to PT infants particularly in very preemies. However, the IgG titres of anti-Dtx and anti-PT were similar among the groups (Figure 4.2).

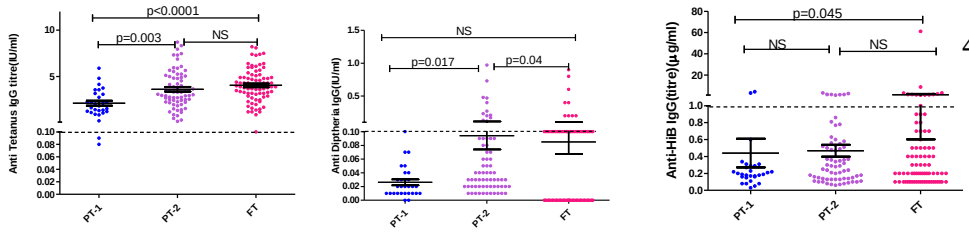
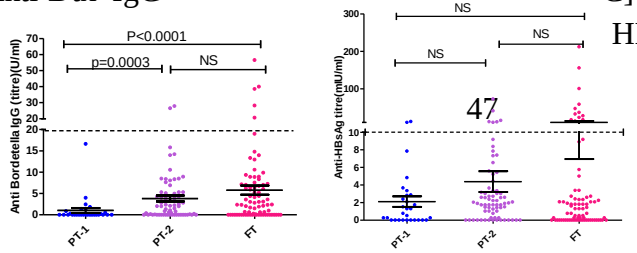


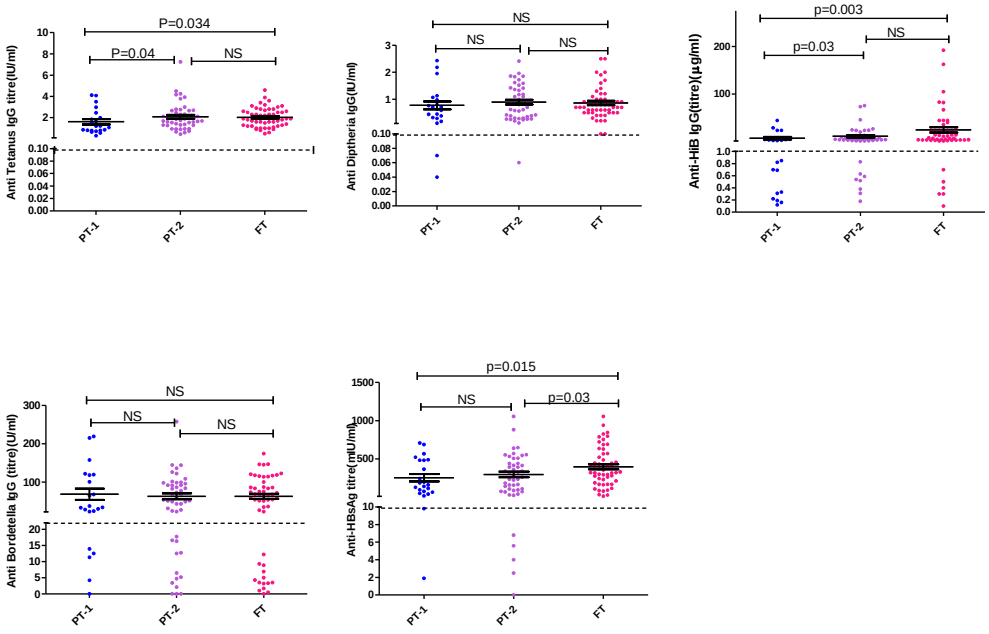
Figure 4: Scatter dot plots showing geometric mean concentration of immunoglobulin G (IgG) against five component antigens, A] Anti-Ttx IgG B] Anti-Dtx IgG C] Anti-Hib IgG D] Anti-PT IgG E] Anti-HBs IgG (1) at baseline (before



vaccination) the age of 4-6 wk and (2) after one month of pentavalent vaccine at the age of 20-24 wk.

(1)

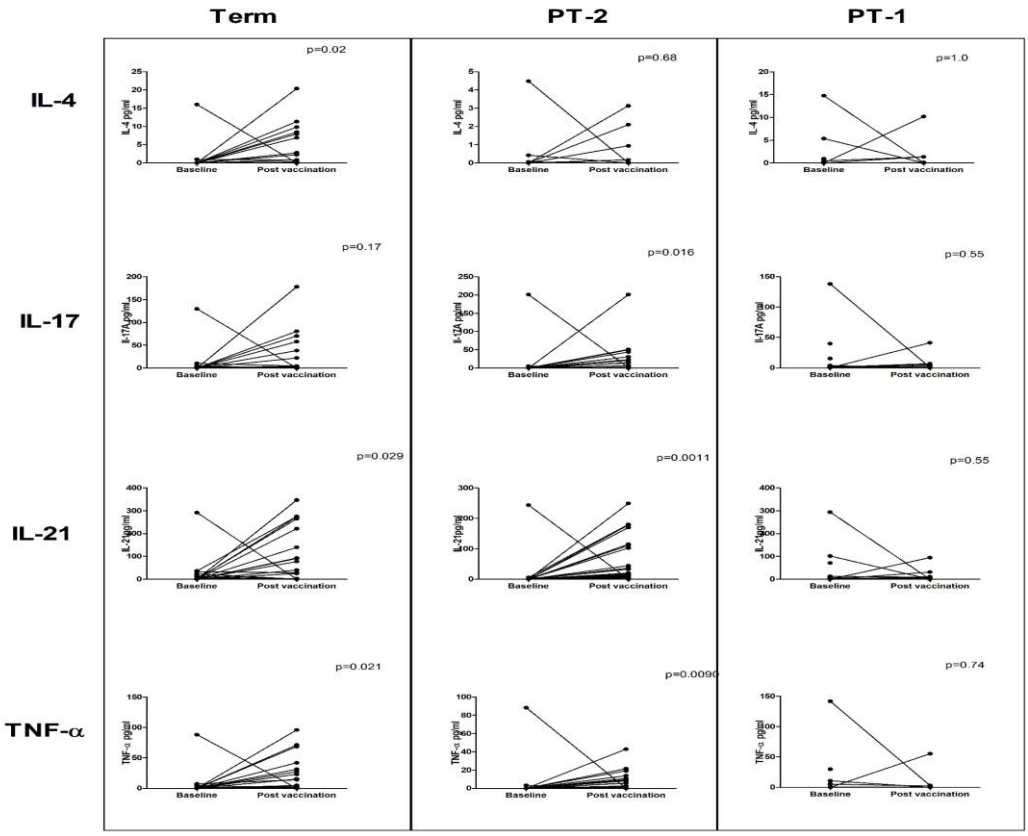
(2)



Plasma cytokine profiles pre and post-pentavalent vaccination: For this, cytokine profiling was carried out using cytometric bead array with 18, 36 and 33 paired plasma samples of pre and post vaccination from PT-1, PT-2 and FT infants respectively. Among Th-1 cytokines, TNF-α levels were significantly higher in PT-2 as compared to PT-1 infants (p=0.03) at enrolment visit. The levels of IL-10, a Th-2 cytokine were higher in PT-1 as compared to PT-2 (p=0.014) and FT (p=0.001) infants at enrolment visit. Post vaccination, IL-10 levels were still higher in PT-1 as compared to PT-2 infants. With respect to other cytokines, at baseline visit and post vaccination visit, there was only marginal difference without any statistical significance among the study groups. But, when the cytokine levels at pre and post vaccination visits were compared in the same study group (Intragroup comparison), IL-21 and TNF-α levels were observed to be significantly higher at post vaccination visit in PT-2 and term infants. Whereas,

significantly higher levels of IL-4 cytokine at post vaccination visit was observed in term infants only (Figure 5).

Figure 5: Line diagrams showing intra group comparison of plasma cytokine profile at pre vaccination (baseline) and post vaccination visit.



Conclusions: Significant low percentage of CD4 T cells and antigen presenting cells such as myeloid DC, plasmacytoid DC and monocytes in pre-term infants as compared to term infants at enrolment visit. At follow up visit, the frequencies of CD4, CD8 T cells and pDC in very preemies were not reached to the levels to term infants, indicates a long-lasting effect of gestational age on immune system.

More than 95% of all infants (irrespective of gestational age) were successful to develop seroprotective titres against Tetanus and Diphtheria toxoids, Hepatitis B surface antigen, and HiB.

Only 70-76% of the infants were able to develop seroprotective titers against Bordetella antigen irrespective of gestational age.

3.**Title:** Norovirus surveillance among children with non-rotavirus associated gastroenteritis in Pune, India (**Project ID**: CD/18/3/E)

Funding: Centers for Disease Control and Prevention (CDC), USA and intramural support from Bharati Vidyapeeth; **Duration:** January 2018 - December 2019; **Sanctioned Amount**:

CDC, USA (Reagents for rotavirus and norovirus testing) and Bharati Vidyapeeth (Rs. 5 lakhs); **Investigators:**
PI: Dr. Ruta Kulkarni; **Co-Investigators**: Dr. V. Kalrao, Dr. S. Mankar, Dr. M. Sangamnerkar; **Human Ethical Approval**: IEC/2017/32 renewed as IEC/2018/47

Work done: This project was initiated in January, 2018. Stool samples are being collected from sporadic cases of acute gastroenteritis among children (≤5 years of age) getting treatment at three hospitals at Pune (Bharati hospital, Mankar hospital and Chinmay hospital).

During January to December 2018, a total of 207 stool samples were collected and 101 (48.8%) were found to be positive for rotavirus. On testing of the remaining 106 rotavirus-negative samples for norovirus, 19 (17.9%) were found to be positive. Of the 19 norovirus-positive samples, 17 were genotyped while 2 remained non-typeable. The genotype distribution of the 17 samples was as follows: GII.P16-GII.4 (n=10), GII.Pe-GII.4 (n=3), GII.P16-GII.3 (n=2), GII.P16-GII.13 (n=1), GII.P7-GII.6 (n=1).

Our result indicates that during 2018, norovirus prevalence among children with non-rotavirus associated gastroenteritis in Pune was found to be 17.9%. Circulation of 5 different genotypes was observed in this population with GII.P16-GII.4 being predominant (58.8%). During January to June 2019, 70 samples have been collected. Testing of these samples for rotavirus and norovirus are in progress.

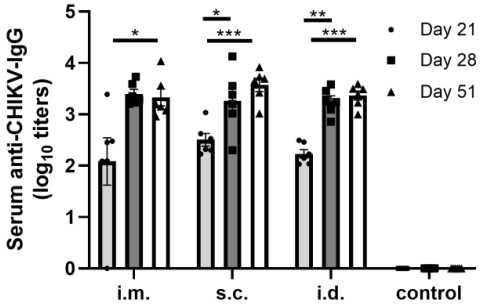
4. **Title:** Evaluation of different adjuvants for development of potent chikungunya vaccine (**Project ID**: CD/18/4/E)
Funding: DST-SERB**; Duration:** May 2018 – May 2021**; Sanctioned Amount:** Rs. 32.2 Lakhs
Investigators: PI: Dr. Harshad Padmanabh Patil; **Ph.D. Student**: Ms. Mrunal Gosavi; **Animal Ethical Approval:** BVDUMC/1890/2018/002/019

Work done: CHIKV virus was propagated on Vero cell line. Cell supernatant was collected and inactivated using 0.1% β-propiolactone. It was concentrated using diafiltration and resuspended in phosphate buffer saline. Complete inactivation of CHIKV was confirmed by observing Vero cells for the absence of cytopathic effect (CPE). Purity of the inactivated CHIKV was checked using SDS-gel electrophoresis and protein concentrations were determined using Folin-lowry assay.
In-vivo experiment was performed in 6-8 weeks old female BALB/c mice. Mice (n=6/experimental group) were immunized twice via the intramuscular (i.m.), intradermal (i.d.) or subcutaneous (s.c). route, at an interval of 3 weeks using 2.5 µg of inactivated CHIKV. Mice were sacrificed one month (day 51) after second dose. Blood was collected on day 21, 28 and at sacrifice. Anti-CHIKV-IgG, -IgG1 and IgG2a were quantified using ELISA. Quality of antibodies was checked using plaque reduction neutralization assay.

CHIKV specific IgG response

We found that single administration of 2.5 µg of inactivated virus induced anti-CHIKV-IgG after first dose which increased more than 10 times after second dose irrespective of the delivery routes (Figure 6). Moreover, antibody titers remained same even after one month post second dose.

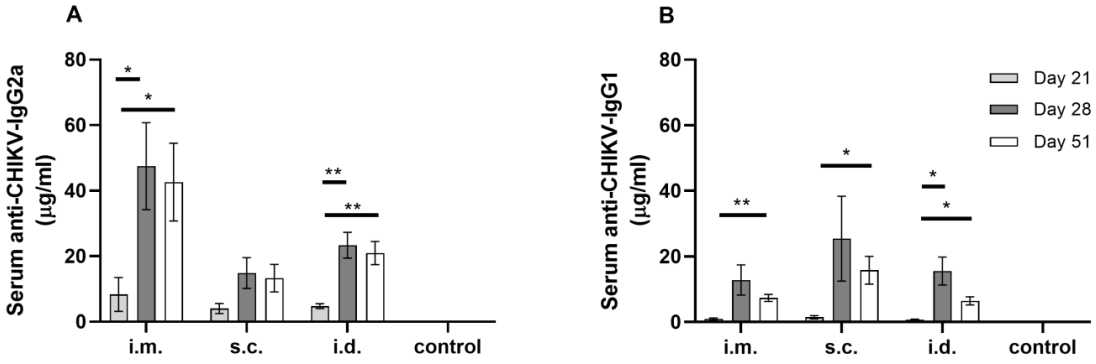
Figure 6: Inactivated CHIKV specific IgG responses in serum collected on days 21, 28, and 51. Mean group titers calculated from individual titers are depicted. Levels of significance are presented as *p < 0.05, **p < 0.01 or ***p<0.001.



Phenotype of CHIKV specific antibody response

Quantification of CHIKV specific IgG subclasses is important to understand the quality of antibody response after immunization. i.m. delivery of inactivated-CHIKV induced highest amount of IgG2a antibodies followed by i.d. and s.c. route (Figure 7A). On the contrary, s.c. delivery elicited highest amount of IgG1 (Figure 7B) while no difference was found in antibody titers between i.m. and i.d. group.

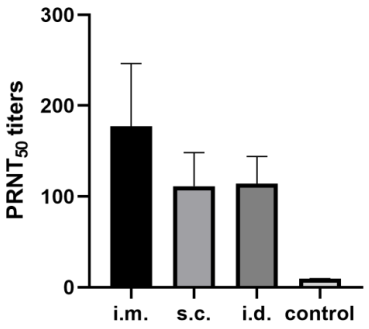
Figure 7: Phenotype of antibody response after immunization with inactivated CHIKV. (A) IgG1 and (B) IgG2a levels are shown as µg per ml. Levels of significance are presented as *p < 0.05, **p < 0.01.



Functional potential of CHIKV specific antibodies

The functional potential of IgG antibodies to neutralize CHIKV was analyzed by performing plaque reduction neutralization test (Figure 8). All the groups induced PRNT titers greater than 10 which are considered protective. i.m. group showed a trend towards increased PRNT titers but no significant difference was observed among different delivery routes.

Figure 8: CHIKV specific neutralizing antibodies ($PRNT_{50}$ titers) in mice immunized with different delivery routes.



5. **Title:** Development of potent adjuvanted respiratory syncytial virus vaccine for mucosal delivery (**Project ID**: CD/18/5/E)
Funding: Wellcome-DBT India Alliance; **Duration:** January 2019 - December 2023; **Sanctioned Amount:** Rs. 1.69 crore; **Investigators: PI:** Dr. Harshad Padmanabh Patil; **Animal Ethical Approval**: BVDUMC/1881/2018/002/010

Background: RSV is a highly contagious respiratory virus responsible for over 33 million new acute lower respiratory infection episodes per year in children under the age of five, most occurring in the first year of life. Of these, >3 million require hospitalization. More than 99% of the deaths occur in developing counties. Currently, there is no approved vaccine for RSV prevention. Treatment with monoclonal antibody prevents RSV associated complications; however, the prohibitive cost does not allow use in the developing countries. RSV vaccines under clinical investigation are administered by injections or intranasally. Injectable immunization fails to induce mucosal immunity while pre-clinical results of adjuvanted nasal vaccines are promising but there is a risk of Bell's palsy associated with it. Alternative to systemic and nasal immunization could be vaccine delivery via sublingual or pulmonary route in children. However, overcoming the Th2 microenvironment in respiratory tract remains challenge. Recognition of two PRR ligands by single cell is shown to alter molecular programming of innate immune cells and enhance Th1 response. Plan of the current study is to evaluate RSV-virus-like-particle vaccine together with chimeric adjuvants that are recognized by two PRR ligands for immunogenicity after sublingual or pulmonary delivery in mice and using system immunology.

Objectives:
Production of candidate RSV vaccines, consisting of VLPs plus different combinations of adjuvants
Determination of the immunological and protective properties of these vaccine candidates in mice
Evaluation of the effects of these vaccine candidates on human PBMC or PBMC-derived cells

Work done: Approval has been obtained from Institutional Biosafety Committee and Institutional Animal Ethics Committee. RSV virus A2 strain has been obtained from American Type Culture Collection (ATCC). The RNA of obtained virus was subject to whole genome sequencing. High-quality reads mapped against RSV reference genomes confirmed it to Human respiratory syncytial virus with 99.65% homology. Primers are designed and procured for cloning of M, G, F and structural protein sequence of RSV in plasmids of interest to obtain respective proteins or RSV-VLP.

6.**Title:** Platelet derived exosomes and their role in endothelial dysfunction in dengue infection (**Project ID:** CD/18/6/E)
Funding: DBT-BioCARe; **Duration:** March 2019 – March 2022; **Sanctioned Amount**: Rs. 46.4 Lakh; **Investigators: PI** - Dr Shubham Shrivastava; **Co-Investigators** - Dr Deepak G Bhosle (Bharati Vidyapeeth Medical College); **Human Ethical Approval**: IEC/2019/15

Background: Dengue is the most common mosquito borne viral disease caused by one of the four dengue virus serotypes. Severe dengue is associated with increased vascular permeability, hypovolemia due to plasma leakage and death. In dengue infection, critical phase of plasma leakage lasts for 24-48 hr after the period of peak viremia suggesting the involvement of host immune response. Recent evidence suggests that platelets on interaction with leukocytes initiate signaling pathways to exert biological functions such as, release of α-dense granules and exosomes. Enhanced platelet activation is associated with disease severity in dengue patients. Moreover, increased thrombocytopenia is reported to be associated with clinically significant vascular permeability in acute dengue infection.
Platelets contain several molecules, including mRNA, microRNA, growth factors, cytokines and chemokines. Platelets are known to adhere to the endothelium in case of any damage, however, how they dysregulate the function of endothelium in dengue infection is unknown. During viral infection, various cell types release exosomes in circulation. Exosomes play a crucial role in cell to cell communication by carrying functional mRNA and microRNA. Origin and content of exosomes carrying microRNAs during dengue infection is not yet explored. This study will evaluate the role of platelet derived exosomes in endothelial dysfunction during dengue infection.

Objectives:

- To investigate the microRNA expression profiles of platelet-derived exosomes in longitudinal samples of dengue patients with different clinical presentations.
- To determine the role of platelet-derived exosomes and exosome associated microRNAs in endothelial dysfunction.

Work done: Approval has been obtained from Institutional Biosafety Committee and Institutional Human Ethics Committee. Human Umbilical Vein Endothelial Cells (HUVEC) has been purchased from American Type Culture Collection (ATCC).

7.**Title**: Establishment of National Centre for Immunogenicity Testing, NCIT to evaluate vaccines in clinical trials (Project ID: CD/18/7/E)
Funding: DBT-BIRAC (Under National Biopharma Mission); **Duration**: March 2019 – March 2023
Sanctioned Amount: Rs. 16 crore; **Investigators**: PI - Dr A C Mishra; **Co-Investigators** – Dr. Vidya Arankalle, Dr. Shubham Shrivastava, Dr. Harshad Patil, Dr. Ruta Kulkarni and Dr. Divya Tiraki; **Human Ethical Approval**: IEC/2019/33
Background: India has strong institutions with robust R&D pipeline of vaccine development. Presently, majority of tests required for vaccine evaluation are available with research facilities or institutions in the country. However, these research institution facilities cannot meet rigid regulatory requirement due to various in-built constraints. In addition, Indian manufacturers acquire many technologies from various international sources. After technology acquisition, vaccine development requires extensive clinical evaluation to prove clinical efficacy. This requires rigid regulatory compliance which needs huge safety and immunogenicity data.
We have many GLP laboratories providing quality pre-clinical safety data. However, GCLP compliant laboratory to perform immunogenicity testing for the evaluation of vaccines in clinical trials are not available. Often blood or plasma samples have to be shipped abroad. Testing abroad is not only expensive but to get regulatory approvals for shipping of samples is cumbersome and time consuming. Therefore, India needs a State of Art center to provide comprehensive immunogenicity testing services to our vaccine manufacturers. Viral vaccine facilities require both GCLP as well as Biosafety compliant laboratories. This project will provide unique facility that will meet long pending need of vaccine manufacturers in our country.

Objectives:
Establishment of GCLP laboratories for immunogenicity testing of vaccines
Setting up of dedicated Biosafety 2 and 3 laboratories compliant to both Biosafety and GCLP requirements.
Acquisition, standardization, validation and finally accreditation of the tests required for immunogenicity testing of vaccines
Creation of self-sustainable business model, capable of absorbing new technologies and maintain pace with newer developments in the field

Work done: Approval has been obtained from Institutional Biosafety Committee and Institutional Human Ethics Committee for the project. Recruitment of staff was done and construction of BSL2 and BSL3 laboratories has been initiated.

8. **Title:** Dynamics of maternally acquired anti-dengue antibodies in infants (**Project ID**: CD/18/1/I)
Funding: Intramural; **Duration:** April 2017 - March 2019; **Sanctioned Amount**: NA; **Investigators:** PI: Dr. Shubham Shrivastava; **Co-PI/ Co-Investigators**: Dr. V. A. Arankalle,

Dr. A. C. Mishra (IRSHA), Dr. Nandini Malshe, Dr. S. Lalwani (Bharati Vidyapeeth Medical College); Ph.D. Students: NA; **Human Ethical Approval**: Ref: BVDU/MC/55

Work done: This study was conducted to assess the seroprevalence of IgG antibodies to dengue viruses in cord blood and at $\leq$ 3, 6, 9, 12 and 15 months of age among the Indian infants. Anti-DENV IgG positivity gradually reduced from birth and was lowest at the age of 9 months.

A total of 57 IgG positive samples were tested for the presence of neutralizing antibodies (Table 1). At birth, all 22 infants (100%) were positive for neutralizing antibodies against 3 or 4 DENV serotypes. There was sharp decline in the proportion of infants positive for neutralizing antibodies against 3 or 4 serotypes to 42.9% at 6 months of age. All four IgM positive infants at 9 months, 12 months and 15 months of age contained neutralizing antibodies against all 4 serotypes. At 15 months of age, 2 infants were exposed to recent dengue infection with high titered IgG antibody and the infecting serotype was DENV-3 and DENV-4.

At birth (cord blood), highest mean titers was recorded against DENV-2 (3091.47) followed by similar lower levels for DENV-3 (548.61) and DENV-4 (511.84); lowest against DENV-1 (228.64). Neutralization antibody titers against DENV-1/2/3/4 were reduced to 38.27, 313.17, 159.57, 111.73 in 3 month-old and to 19.44, 93.31, 61.36, 38.96 in 6 month-old infants.

Table 1: Distribution pattern of dengue serotype specific neutralizing antibodies ($PRNT_{50}$) among the infants examined at different ages

Age groups (no. of samples tested)	Monotypic (%)	Bi-typic (%)	Tri-typic (%)	Quadro-typic (%)
Cord Blood (n=22)	0	0	3 (13.6)	19 (86.4)
3 month (n=6)	0	1 (16.7)	0	5 (83.3)
6 month (n=14)	1 (7.1)	7 (50)	2 (14.3)	4 (28.6)
9 month (n=3)	0	0	0	3 (100)
12 month (n=5)	0	0	2 (40)	3 (60)
15 month (n=7)	0	0	3 (42.9)	4 (57.1)

Conclusions: High rate of transfer of maternal antibodies was evident in infants with 71.3% anti-dengue seropositivity at birth.
Anti-dengue IgG antibody positivity was found to be lowest at 9 months of age.
Neutralizing antibody titers against all 4 serotypes were reduced to lowest levels in 6-month old infants.

9.Title: High throughput profiling of microRNAs and their roles in Dengue virus pathogenesis (**Project ID:** CD/18/2/I)

Funding: Intramural; **Duration:** October 2017 - September 2018; **Sanctioned Amount**: NA; **Investigators:** PI: Dr. Shubham Shrivastava; **Co-PI/ Co-Investigators**: Dr. A. C. Mishra (IRSHA); **Human Ethical Approval**: BVDUMC/IEC/94

Work done: The role of host microRNAs (miRNA) as potential biomarkers in dengue infection is not well characterized. For this, miRNA profiling was carried out using serum samples of dengue patients with different clinical presentations – control (2 pools, n=8), dengue illness without warning signs (WOS, 4 pools, n=16), dengue illness with warning signs (WS, 4 pools, n=20) and severe dengue (SD, individual sample, n=5).
A total of 372 miRNA expression profiles were analyzed based on disease severity. In compared to healthy controls, WOS group contained 79 upregulated and 152 downregulated and WS group contained 62 upregulated and 181 downregulated miRNAs. In contrast to the findings in WOS and WS groups, SD group showed upregulation of 156 and downregulation of 97 miRNAs. In SD infection, expression of 2 miRNAs (miR-150-5p and miR-210-3p) was significantly increased as against WS patients suggesting their role in disease severity. Moreover, when miRNA expression profiles were compared with different disease categories in adult patients, 4 additional miRNAs (miR-1280, miR-191-5p, miR-3646, miR-378g) along with miR-210-3p were significantly increased in SD than in patients with WS.
miRNA expression profiles were analyzed based on type of dengue infection, primary vs secondary. 6 miRNAs (miR-29a-3p, miR-139-5p, miR-21-5p, miR-181a-5p, miR-375 and miR-374a-5p) were significantly upregulated and only one miRNA, miR-221-3p was downregulated in patients with WS after secondary dengue infection.
On further analysis, expression profiles of 4 miRNAs (miR-2276-3p, miR-523-3p, miR-433-3p, miR-375) were remained elevated and expression profiles of 3 miRNAs (miR-27a-3p, miR-122-5p, miR-25-3p) were downregulated with increase in disease severity (Table 2).

Table 2: Fold regulation of upregulated and downregulated miRNAs in different disease categories following secondary dengue infection in comparison to healthy controls.

Upregulated miRNAs	WOS	WS	SD
miR-2276-3p	1.89	6.45	10.88
miR-523-5p	1.37	2.06	6.75
miR-433-3p	1.45	2.35	7.17
miR-375	1.91	14.92	40.96
Downregulated miRNAs	WOS	WS	SD
miR-27a-3p	-1.401	-5.37	-6.547
miR-122-5p	1.57	-2.802	-4.175
miR-25-3p	-1.19	-5.44	-10.702

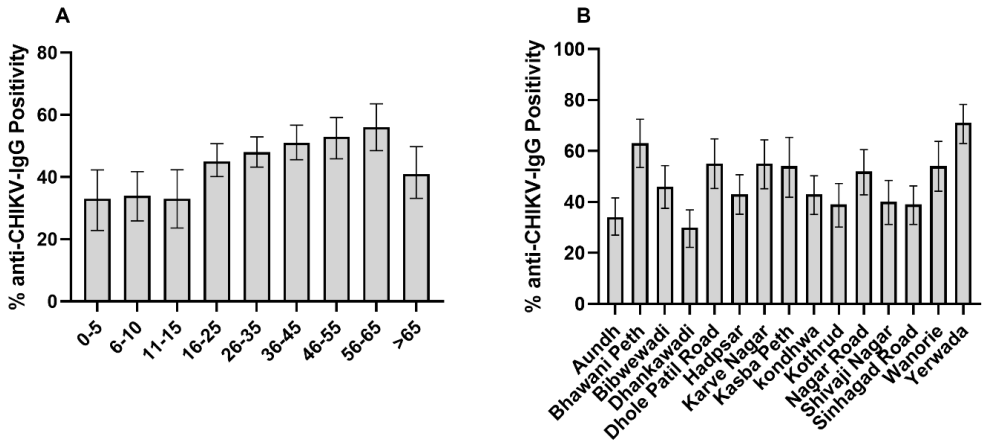
Conclusions: Biomarker potential of 7 miRNAs (miR-2276-3p, miR-523-3p, miR-433-3p, miR-375, miR-27a-3p, miR-122-5p, miR-25-3p) should be explored for disease severity in dengue infection.

10.**Title:** Age-stratified prevalence of anti-chikungunya-IgG antibodies in Pune, India (Project ID: CD/18/3/I)
Funding: Intramural; **Duration:** July 2018 - December 2019; **Sanctioned Amount:** NA; **Investigators:** PI: Dr. Vidya A. Arankalle; **Co-PI/ Co-Investigators:** Dr. Harshad P. Patil, Dr. A.C. Mishra; **Human Ethical Approval:** IEC/2017/04, renewed IEC/2018/11

Background: In the absence of robust surveillance, true estimates of disease burden of CHIKV are still unknown. An approach would be to assess population groups for prior exposure to the virus by testing for IgG antibodies. With this view, retrospective samples collected during 2017 for age-stratified DENV serosurvey study were used (Mishra et al. 2018). As both DENV and CHIKV viruses are transmitted by the same vector and are related to monsoon season, we decided to subject these samples to anti-CHIKV-IgG testing.

Work done: Prevalence of anti-CHIKV-IgG antibodies in Pune population:
Of the 1904 individuals screened, 934 (49.05%) were males and 966 (50.76 %) females. Adults contributed to 83.08 % (n=1582) while 323 (16.96%) were children ≤ 15yeras age. The overall seropositivity was 46.37% with median age of 35 years. Figure 9A depicts age-wise anti-CHIKV antibody positivity in Pune population. One third of the children <5years age were already exposed to the virus. The positivity was similar till the age of 15 (p>0.9). At 16-25years, a significant rise was recorded (45%, p=0.026-0.038). The positivity varied between 48-56% till the age of 65. Exposure of elderly population (>65years) was lower than those aged 56-65years age (41%, p=0.01). There was a distinct difference in CHIKV antibody positivity among different wards of Pune city (Figure 9B), from the lowest in Dhankawadi ward (15%) to highest in Yerwada (61%). 4/15 wards exhibited > 50% antibody positivity.

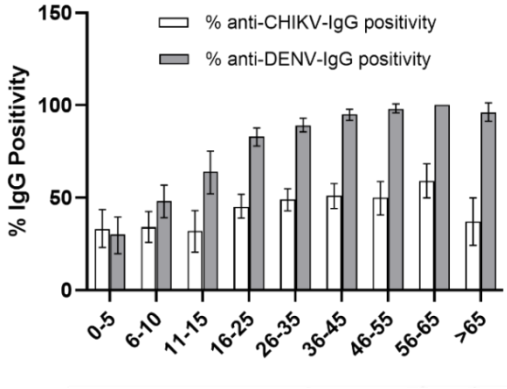
Figure 9: (A) Age wise prevelance of anti-CHIKV antibodies (n=1904). (B) Percentage of participants tested positive for anti-CHIKV-IgG antibodies in 15 municipal wards of Pune city. Error bars indicates 95% confidence interval.



Comparison of CHIKV and DENV IgG antibody positivity:

We next compared the positivity rates of anti-CHIKV and anti-DENV IgG antibodies (Figure 10). Overall, evidence of prior exposure to CHIKV was seen in 576/1260 (45.7%) samples. Of these 89.6% were exposed to DENV as well. Except for children <5years age (p=0.73), prevalence of DENV antibodies was higher than CHIKV in all the other age groups (0.038-<0.001). The antibody positivity patterns were different for CHIKV and DENV. No association between CHIKV and DENV seropositivity was evident.

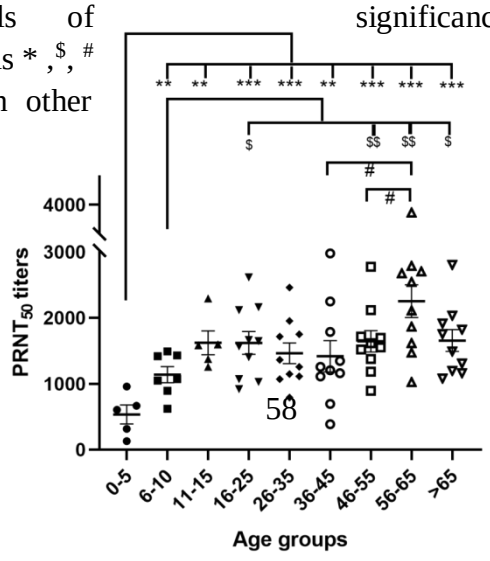
Figure 10: Age wise distribution of percentage of participants tested positive for CHIKV and DENV IgG (n=1260).



Neutralization potential of anti-CHIKV-IgG antibodies

To determine the neutralization potential of anti-CHIKV-IgG antibodies induced after CHIKV infection, 5 samples of each age group were pooled and CHIKV specific $PRNT_{50}$ titers were determined (Figure 11). Children between age group 0-5 had the lowest $PRNT_{50}$ titers with mean titer of 534.84 (95% CI: 253.43 to 816.25). The titer gradually increased with age and children in age group 11-15 had $PRNT_{50}$ titer of 1620 (95% CI: 1267.76 to1973.60) that remained consistent till age group >65. In adults, the mean $PRNT_{50}$ titer was 1669 (95% CI: 1509.86 to1839.52) and ranged between 1417 (age group 36-45, 95% CI: 994.78 to 1919.90) till 2252 (age group 56-65, 95% CI: 1763.19 to 2740.58). Except for age group 56-65, no difference in the $PRNT_{50}$ titer was observed from age group 11-15 till >65.

Figure 11: CHIKV specific neutralization antibodies and age wise distribution of $PRNT_{50}$ titers (n=77 pools). Levels of significance are presented as*, $, # p < 0.05, ** p < 0.01. Symbols * ,$, # are used to compare age group 0-5, 6-10 or 56-65 with other age groups respectively.



Conclusions: CHIKV is highly endemic in Pune city even after 11 years post-resurgence. 68-97% population was already exposed to either of DENV or CHIKV in Pune city. Age dependent increase in neutralizing antibody titers against CHIKV was observed

Centre for Innovation in Nutrition Health Disease (CINHD)

1. Title: ICAR -AICRP- Linseed Value Addition Centre (**Project ID: CINHD/18/1/E**
Funding: ICAR, New Delhi; **Duration:** April 2015 onwards; **Investigators:** Dr. Anand A. Zanwar; **Sanctioned Amount:** Total 73.44 Lakh (2015-18), 28.47 Lakh (2018-19)

Background:

Broad objective is linseed value addition. The objectives for 2018-19 were planned and approved during Annual Linseed Group meeting held at Birsa Agricultural University, Ranchi during 10 – 12 August, 2018.

Objectives for 2018-19:

A. Blending of linseed oil with edible oil
B. Development of omega-3 enriched energy bar
C. Development of lignan rich linseed hull powder

Work done (objective-wise):

A. Blending of linseed oil with edible oil

Objective: To study oxidative stability of blended linseed oil with added antioxidants.

Materials and methods:

Various edible oils and their linseed oil blends: palm olein, coconut oil, rice bran oil, mustard oil, with added antioxidants namely Ascorbyl Palmitate (AP - 500 mg/kg) and Tertiary butyl hydroquinone (TBHQ - 120 mg/kg) were subjected for oxidative stability for period of 8 months.

Results:

Efficacy of AP was significant in controlling peroxidation of all blends when compared to TBHQ and acid value was also within acceptable limit. To know the effect of AP and TBHQ on peroxidation and acid value, this experiment will be continued as the base oil itself has varied stability duration. AP showed very significant effect in controlling the shelf life of blended oil in coconut and other blends also. Hence this experiment also need to be continued for next year to see the effect of antioxidants till 15-18 months.

B. Development of omega-3 enriched energy bar

Methods:

Four different combination of energy bars were prepared i.e. A-control (without omega-3 FA), B-linseed emulsion, C-linseed emulsion + whey protein and D-linseed oil. These bars were evaluated for fatty acid composition, oxidative stability, and texture profile.

Results and discussion:

The control energy bar did not contain linseed or linseed oil. Roasted linseed were added in all three experimental groups. Further linseed oil or linseed emulsion were added in group B, C and D as major source of omega-3 fatty acid. Protein constitute an important health component of energy bar. Hence in group C, 80% whey protein concentrate was added as source of protein. As expected there was very significant alteration in PUFA content in all experimental groups as compared control group bars. Further very healthy omega-6 to 3 ratio 0.86:1 to 0.95:1 was attained. In the present trial it is important to note that, addition of linseed/linseed oil/linseed emulsion lead the reduction of unhealthy SFA and significant increase in PUFA content including omega-3 fatty acid (alpha-linolenic acid) (Table 1). There was insignificant alteration in peroxide value, acid value and free fatty acid content in experimental groups as

compared to control group (Table 1). Breaking strength using compression test (load taken to break the energy bar at 1st compression) revealed there was non-significant alteration in group B and C as compared to control (group A), however significant reduction was noted in group D as compared to group A. Deflection test (deflection to break the sample) revealed non-significant alteration in all experimental group as compared to control (Table 1).

Table 1: Fatty acid composition, oxidative stability, texture profile of omega-3 energy bar

Parameters	Control (A)	Linseed emulsion (B)	O-3 emulsion + Whey protein (C)	Linseed oil (D)
Fatty acid profile				
SFA %	78.18±0.45	60.89±0.19	63.44±0.78	62.55±0.47
MUFA %	12.41±0.85	14.67±0.69	13.21±0.15	13.99±0.40
PUFA %	9.35±0.39	24.38±0.50	23.29±0.61	23.40±0.07
O-3 %	0.00±0.00	12.86±0.48	12.52±0.37	12.05±0.84
O-6 %	9.35±0.39	11.52±0.99	10.77±0.98	11.35±0.92
O-9 %	12.41±0.85	14.67±0.69	13.21±0.15	13.99±0.40
O-6:O-3	-	0.90±0.11	0.86±0.10	0.95±0.14
ALA (g/100g)	00	3.14	3.08	2.88
Oxidative stability				
Peroxide value	1.03±0.11	1.73±0.05	1.90±0.00	1.06±0.057
Acid value	1.28±0.025	1.38±0.03	1.19±0.045	1.38±0.00
Free fatty acid	0.24±0.005	0.34±0.009	0.24±0.00	0.28±0.02
Texture profile				
Breaking strength	17.59±5.20	14.51±1.37	14.85±1.60	4.65±0.82
Deflection test	1.548±0.56	1.28±0.15	1.39±0.45	1.36±0.35

Note: texture profile analysis was carried out at CSIR-CFTRI, Mysore

In conclusion, considering overall parameters energy bars prepared using linseed emulsion (group B and C) were superior to control (group A). In group D i.e. bar prepared using linseed oil were more stable, but did not performed well in compression test. The fatty acid profile established that bars (B, C, and D) were all significantly enriched with marked changes in omega-6 to 3 ratio.

C. Development of lignan rich linseed hull powder

In order to concentrate the lignan content, various treatment such removal of fat, mucilage and separating hull from whole seed were carried out. De-hulling was carried out after pulverization using laboratory sieves, mucilage removal was carried out using hot extraction method and defatting was carried out using soxhlet extractor. Different fractions were subjected for lignan content determination by HPTLC. It was preliminary trial, lignan content varied from 2.92 to 9.08 mg/g. To start with lignan content in linseed powder was 5.04 mg/g, hull powder 6.79 mg/g and de-hull powder recorded 2.92 mg/g. De-fatting and de-hulling resulted in significant improvement in lignan content as compared to whole powder i.e. 8.67 mg/g. Further removal of mucillage from de-fatted hull powder resulted in further improvement in lignan content i.e. 9.08 mg/g (Table 2). In conclusion, removal of fat and mucilage and separating hull from whole seed resulted in significant improvement in lignan content. It needs

to be noted that, as separation of hull and mucilage was carried out manually hence there was some loss of lignan content. Hence further improvement need to be carried out using mechanical de-huller to get better yield of lignan.

Table 2: Lignan content in different linseed samples

Sr. no.	Name of sample	Lignan content (mg/g)
01	Whole seed powder with fat	5.04±1.27
02	Hull powder with fat	6.79±1.39
03	De-hull powder with fat	2.92±0.72
04	Whole seed powder without fat	6.66±1.28
05	Hull powder without fat	8.67±1.43*
06	De-hull powder without fat	4.61±0.95
07	De-mucillaged whole seed powder without fat	8.37±0.88*
08	De-mucillaged hull powder without fat	9.08±0.64**
09	De-mucillaged de-hull powder without fat	4.17±1.95

$p<0.05$ and $p<0.01$ as compared to whole seed powder with fat.

2. **Title:** Evaluation of efficacy of novel stabilized omega-3-fatty acid and antioxidants formulation for the prevention and treatment of metabolic syndrome (**Project ID:** CINHD/18/2/E**)**

Funding: DST-SERB; **Sanctioned amount:** 40.36 Lakh; **Investigators:** PI: Dr. Anand Zanwar; **Duration:** June 2017 to June 2020; **Ethics Committee approval:** BVDUMC/1888/2018/002/017

Last year formulation containing omega-3 fatty acid along with vitamins and micronutrients was developed through emulsification method. Further formulation was tested for nutritional evaluation as per Food Standard Safety Association of India (FSSAI) guidelines and followed by organoleptic and sensory evaluation studies were carried out to evaluate the acceptability of developed product. This year developed formulation was subjected for characterization, stability evaluation, in vivo acute toxicity study has been carried out. Presently high fat diet induced animal study has been initiated to evaluate the efficacy of emulsified formulations in metabolic syndrome.

Results:

The food emulsion are widely accepted formulations in food and pharmaceutical industries. However major hurdle/challenge is safety and stability of formulation.

- Based on oxidative stability parameters, formulation was found to be stable as all values were within acceptable levels during storage stability study (peroxide value, acid value, free fatty acid content and p-anisidine value) (Fig 1).
- Formulation did not show phase separation at centrifugation tests (stress testing using centrifugation) and repeated freezing and thawing.
- Instabilities such as phase separation, phase inversion, flocculation, creaming and sedimentation was not observed.
- Optical microscopy study revealed stability of formulation.
- No microbial contaminant was observed during storage duration.
- The particle size distribution play key role in product performance i.e. dissolution,

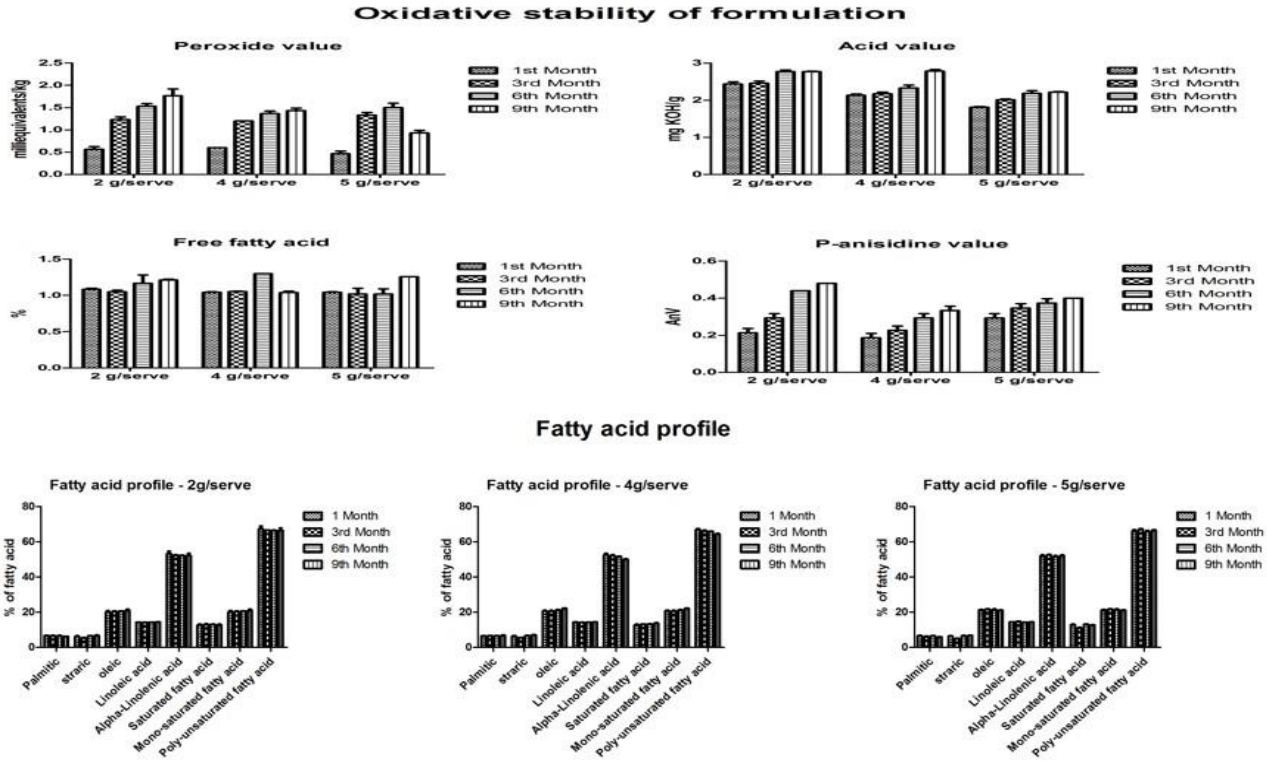
bioavailability, homogeneity, stability, etc. This uniformity and homogeneity of formulations in spite of many ingredients present in the formulation was consistent in various parameters such as colour, dilution test, particle size analysis, optical microscopy.

- Particle size analysis, PDI and zeta potential analysis in *in vitro* stability study further confirmed the stability (Table 3).
- Acute toxicity in animal study recorded no mortality and no gross clinical observations or toxic effect in animals were noted, indicating safety of the formulation.

Table 3: Particle size, PDI and zeta potential analysis of formulations:

Parameters	2 g/serve	4 g/serve	5 g/serve
Particle size (nm)	680.50±88.86	673.83±23.87	798.76±44.51
PDI	0.681±0.18	0.52±0.07	0.438±0.035
Zeta potential (mv)	-27.80±1.38	-26.33±2.20	-26.96±2.25

Figure 1: Oxidative stability study and fatty acid stability study



Conclusion:

- Method of preparation of formulation was optimized on lab scale homogenizer.
- Stability of omega-3 fatty acid ensured.
- Stability of formulation for the period of 9 months assured.
- Nutritive value of final formulation has been ascertained.
- *In vitro* stability study confirmed utility of formulation for oral administration.

3. **Title: Development of infection-resistant urinary Foley catheter** (Project ID: CINHD/16/1/I)
Funding: BVDU, Pune; Investigators/ Co-Is / Co-PIs: Dr. Arnab K. Ghosh; Duration of the project: January 2016 – June 2020

Background: We have aimed to develop a novel antimicrobial composition and method of coating to produce affordable, safe and lubricious antimicrobial coated urinary Foley catheter, which would provide a prolonged and broad spectrum antimicrobial efficacy.
Our previous in vitro studies demonstrated that newly developed latex urinary catheter (AntiBac-L) coated with a novel antimicrobial formulation comprising of chlorhexidine, silver sulfadiazine and curcumin-C3-complex was found to be more effective in preventing adherence of uropathogens like E. coli, S. aureus, K. pneumoniae, P. aeruginosa, S. faecalis, P. mirabilis and C. albicans), when compared to uncoated and commercially available "Bactiguard^{TM}" infection resistant urinary catheters. Here, we have evaluated the surface roughness, capability to resist microbial adherence and subsequent biofilm formation, dry weight of biofilm forming cells and physico-mechanical properties of the uncoated and antimicrobial coated (AntiBac-L) catheter surfaces.

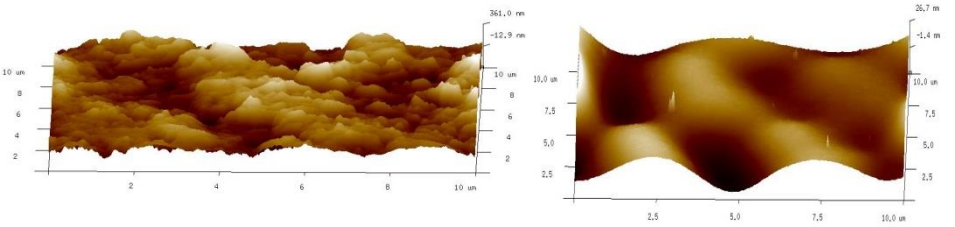
Work done: Atomic force microscopy: Atomic force microscopy (AFM) was carried out to determine surface roughness (Rq) of urinary catheters. Sections (approx 5 X 5 mm) of uncoated and AntiBac-L coated (newly developed antimicrobial coated catheter) were mounted onto metal stubs and surface roughness was evaluated by atomic force microscopy.
Scanning electron microscopy: Uncoated, AntiBac-L coated and commercially available "Bactiguard^{TM}" infection resistant urinary catheter segments (1 cm) were incubated with uropathogenic E. coli and C. albicans cultures separately (10^7CFU/ml) for 24 h. They were washed with 0.1M sodium phosphate buffer, pH 7.2 (SPB), immersed into a fixing solution (Karnovsky) and kept for 24 h at 4°C. Then, they were post-fixed with a solution of 1% osmium tetroxide. Catheter segments were washed again with SPB and dehydrated in a gradient series of ethanol (10%, 30%, 50%, 70%, 90% and 100%). Catheters were then air dried, sputter coated with Au/Pd and imaged using field emission scanning electron microscopy (FE-SEM).
Quantitative measurement of biofilm growth: Uncoated and AntiBac-L coated catheter segments (3cm length) were incubated with C. albicans culture (10^6CFU/ml) at 28°C for overnight. Catheter pieces were kept on transferring daily into fresh growth media inoculated with C. albicans (10^6 cfu/ml). They were removed at 24h, 48h and 72h intervals and gently washed with PBS to remove non-adherent cells. Then, catheter segments were subjected to bath sonication in order to detach biofilm organisms from catheter surface along with vortexing at regular interval. All organisms were collected on pre-weighed cellulose acetate filters (0.22µm pore size). The filters were dried at 37°C, and the dry weights of biofilm forming cells per catheter segment (3cm) were calculated.
Evaluation of physico-mechanical properties of catheter: Physico-mechanical properties like [tensile strength, Young's modulus and elongation at break (%)] of the uncoated and AntiBac-L coated catheters were evaluated using computerized universal testing machine.

Results:

Atomic force microscopy:

The 3D topographic images obtained from AFM study clearly demonstrated that the surface of AntiBac-L coated catheter was smoother than the uncoated catheter (Fig 2). Surface roughness (Rq) of the uncoated and coated catheter was found to be 103nm and 8.2nm respectively.

Fig 2: 3D topographic images of the uncoated and AntiBac-L coated catheter surface



Uncoated catheter AntiBac-L coated catheter

Scanning electron microscopy:

Scanning electron microscopy (SEM) studies have shown that AntiBac-L coated catheter prevents microbial adherence and hence, biofilm formation against uropathogenic E. coli and C.albicans, whereas a heavy microbial adherence has been found on the surface of uncoated and "Bactiguard^{TM}" catheter (Fig. 3 and 4).

Fig.3: SEM images of catheter surfaces challenged against uropathogenic E.coli

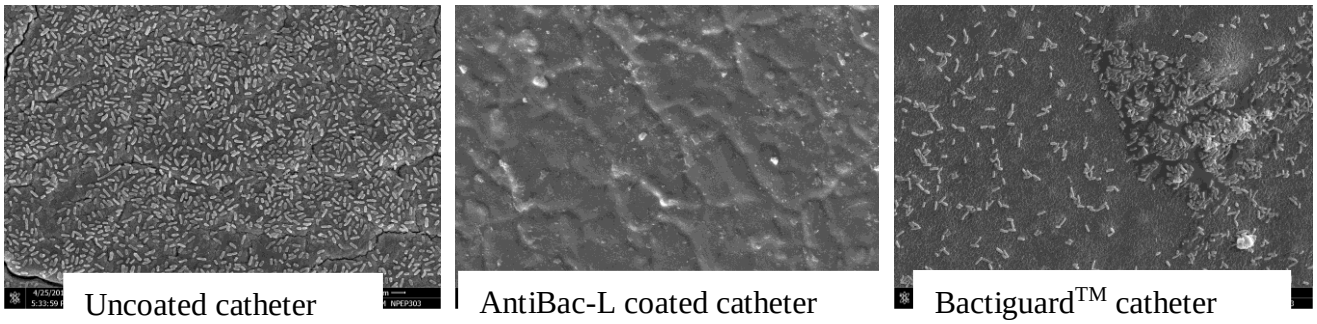
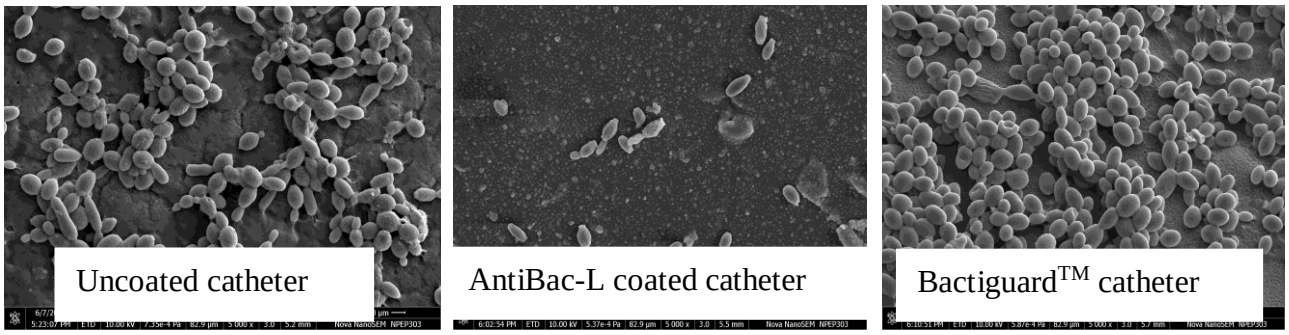


Fig.4: SEM images of catheter surfaces challenged against uropathogenic C. albicans

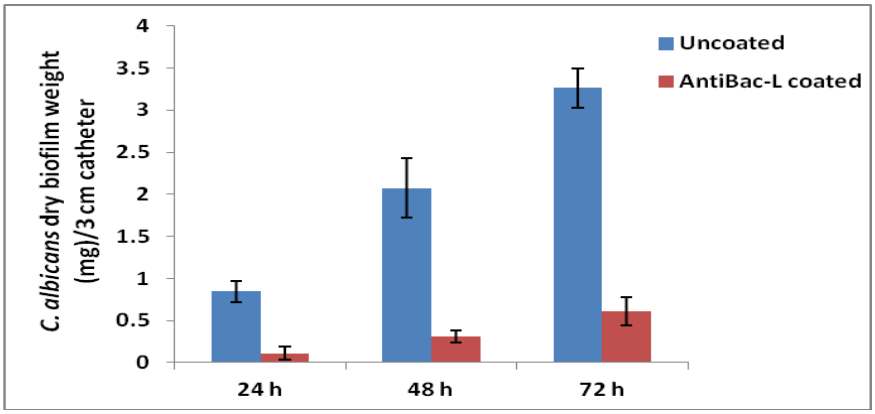


Quantification of biofilm dry weight:

Biofilm dry weight on uncoated and AntiBac-L coated catheter surface was measured at 24h, 48h and 72h interval. It has been observed that the biofilm growth was 0.84 mg, 2.07 mg and 3.26 mg on uncoated catheter surface after 24h, 48h and 72h respectively; whereas in case of

AntiBac-L coated catheter, biofim dry weight was found to be 0.11 mg, 0.31 mg and 0.61 mg after 24h, 48h and 72h respectively (Fig. 6).

Fig 6: C. albicans biofilm dry weight on catheter surfaces



Values are represented as mean ± SD of three independent experiments (n=3)

Evaluation of physico-mechanical properties of catheter:

Physico-mechanical properties of AntiBac-L coated and uncoated catheters have been tested by Universal Mechanical Testing Machine. It has been found that tensile strength (22.02MPa), Young modulus (2.54MPa) and elongation at break (683.33%) of the uncoated catheter were almost equivalent, when compared to tensile strength (23.58MPa), Young modulus (2.62MPa) and elongation at break (705.55%) of AntiBac-L coated catheter (Table 4).

Table 4: Physico-mechanical properties of uncoated and AntiBac-L coated catheters

Catheter type	Catheter size (Fr.)	Physico-mechanical properties of catheter		
		Tensile strength (Mpa)	Young modulus (Mpa)	Elogation at break (%)
Uncoated	16 Fr.	22.02 ± 2.04	2.54 ± 0.13	683.33 ± 10
AntiBac-L coated	16 Fr.	23.58 ± 2.37	2.62 ± 0.16	705.55 ± 7.7

Values are represented as mean ± SD of three independent experiments (n=3)

Conclusions: Atomic force microscopy (AFM) studies have shown that surface roughness of uncoated catheter is 12.5 times higher than the AntiBac-L coated catheter. In other words, the surface of AntiBac-L coated catheter was smoother than the uncoated catheter Scanning electron microscopy (SEM) studies have demonstrated that AntiBac-L coated catheter prevents microbial adherence and biofilm formation against uropathogenic E. coli and C. albicans. C. albicans biofilm dry weights on uncoated catheter surface after 24h, 48h and 72h have been found to be higher compared to AntiBac-L coated catheter surface. Physico-mechanical properties of the catheters coated with antimicrobial agents have remained equivalent, when compared to the uncoated catheters.

4. Title: Development of Chromatographic Method for Quantification of Glycolytic Intermediates and Its Correlation with Enzyme Kinetics in Type – II Diabetes. (**Project ID: CINHD/18/1/I/P)**

Funding: BVDU, Pune; **Investigators/ Co-Is / Co-PIs:** Prof. M. V. Hegde and Prof. Dr. Janhavi R. Rao; **Ph.D. Student:** Ms. Sunita Shivaji Bhise; **Animal Ethics Committee approval:** BVDU/MC/63; **Duration of the project**: Sept 2013 – June 2020

Background: The present study is aimed at exhaustive analysis of glycolysis in type – 2 diabetic erythrocyte to get an insight into alteration in glycolytic pathway.The substrate concentrations of glycolytic intermediates and the kinetic properties of glycolytic enzymes were measured. The substrate kinetic parameters of hexokinase and phosphofructokinase – the key enzymes of glycolysis with irreversible kinetics from type 2 diabetic erythrocyte were compared with erythrocytes of age and sex matched control subjects.

Work done: Protocols for Kinetic studies of Glycolytic enzymes i.e. Hexokinase and Phosphofructokinase in erythrocyte have been standardized. These kinetic studies for patients and controls have been completed. The data was analyzed and interpreted and sent for publication.

Results: Hexokinase activity in the control erythrocytes showed two components: I and II with glucose as the substrate having Km values of 14 and 84 µM and Vmax values of 0.012 and 0.023 nmoles/min/10^6 RBC respectively. By contrast, in the diabetic RBCs exhibited only one component was noted with high Km values of 110 µM ($p< 0.05$) and significantly high Vmax value of 0.034 nmoles/min/10^6 RBC comparable to component II of the control group ($p<0.0001$). In the control RBCs, the derived ^{App}Kcat and ^{App}Kcat/Km values for component I were 1.8 x10^8 and 12.82 and for component II were 3.5 x 10^8 and 4.23 whereas the diabetic RBCs showed ^{App}Kcat of 4.9 x 10^8 ($p<0.0001$) without significant change in ^{App}Kcat/Km values (Table 5).

With ATP as the substrate the hexokinase activity resolved in two components in both the control and diabetic RBCs. The control RBCs showed substrate hexokinase activity with inhibition constant (Ki) of 7 mM. However in the diabetic group no inhibitory effect observed; the activity was increased with increased concentration of ATP. In the control group, for ATP Km value of component I and II were 88 and 312 µM and the corresponding Vmax values were 0.019 and 0.037 nmoles/min/10^6 RBC respectively. Whereas in the diabetic group, the Km of Component I was 46 µM Vs 88 µM ($p<0.0001$) with Vmax of 0.013 nmoles/min/10^6 RBC ($p=0.0005$, lowered by 30 %). By contrast to this, for component II, extensively high Km value was noted (502 µM against 312 µM) with Vmax values comparable to controls. The ^{App}Kcat for component I were 2.8 x 10^8 and 1.9 x 10^8 ($p<0.0001$)in control and diabetic RBCs respectively. However the ^{App}Kcat/Km values showed only marginal increase in diabetic RBCs ($p<0.03$, 4.31 Vs 3.2). For component II ^{App}Kcat values were 5.5 x 10^8 in control with significant reduction to 5.1 x 10^8 in diabetic group ($p<0.0001$). Similarly, ^{App}Kcat/Km also showed remarkable decrease in diabetic RBCs (1.06 Vs 1.81, $p<0.0001$) (Table 5).

Table 5. Kinetic properties of erythrocyte hexokinase in type 2 diabetes

		Component-I		Component-II	
Substrate	Parameter	Control (n=12)	Diabetic (n=40)	Control (n=12)	Diabetic (n=40)
Glucose	K_m (µM)	14.0 ± 0.04	-	84.0 ± 5.3	110.0 ± 6.0*
	V_{max}	0.012 ± 0.001	-	0.023 ± 0.001	0.034 ± 0.001***
	$K_{cat}\times10^5$	1.8 ± 0.02	-	3.5 ± 0.02	4.9 ± 0.02***
	$^{App}K_{cat}/K_m \times10^6$	12.82 ± 1.25	-	4.23 ± 0.41	4.88 ± 0.46 NS
ATP	K_m (µM)	88.0 ± 4.0	46.0 ± 3.1***	312 ± 30.0	502 ± 20.0***
	V_{max}	0.019 ± 0.001	0.013 ± 0.001**	0.037 ± 0.002	0.037 ± 0.002 NS
	$K_{cat}\times10^5$	2.8 ± 0.02	1.9 ± 0.02***	5.5 ± 0.04	5.1 ± 0.04***
	$^{App}K_{cat}/K_m \times10^6$	3.20 ± 0.34	4.31 ± 0.30NS	1.81 ± 0.13	1.06 ± 0.10***

The results are given as mean ± SEM of number of observations indicated in parentheses. *, p <0.05; **, p <0.0005; ***, p <0.0001, NS, Not Significant.

Hill plot analysis of the substrate kinetics data with glucose is presented in Table 2. For glucose, in the control group up to 86 µM glucose concentration one glucose molecule was bound while beyond this concentration two molecules of glucose were bound under experimental conditions. By contrast, in diabetic group one glucose molecule was bound throughout the substrate concentration range. For ATP, in the control group, one molecule of ATP was bound to the enzyme over the entire concentration range. However, in the diabetic group below the transition concentration of 251 µM apparently 0.52 molecules were bound to the enzyme indicating negative cooperativity. However, beyond the transition concentration the enzyme bound to 1 molecule of ATP (Table 6).

Table 6. Hill plot analysis of erythrocyte hexokinase in type 2 diabetes

Substrate	Subject	HiII Coefficient		Transition Concentration (µm)
		n_1	n_2	
Glucose	Control (n=12)	0.81 ± 0.06	1.70 ± 0.03	86 ± 11.7
	Diabetic (n=40)	0.98 ± 0.02	-	-
ATP	Control (n=12)	1.08 ± 0.02	-	-
	Diabetic (n=40)	0.52 ± 0.01	1.34 ± 0.04	251 ± 10.5

The results are given as mean ± SEM of number of observations indicated in parentheses.

Phosphofructokinase activity with F-6-Pas the substrate resolved intoa single component in both control and diabetic group. The Km and Vmax value were 290 µM and 0.27 nmoles/min/10^6 RBC respectively in the control group whereas in the diabetic group the Km

value was significantly higher i.e. 370 µM ($p<0.0001$) with 50% decrease in Vmax ($p<0.0001$, 0.14 Vs 0.27). With ATP, the control group Km and Vmax values were 50 µM and 0.24 units respectively. However, component I of the diabetic group shows substantial decrease (60% decrease) in Km with 29% decrease in Vmax. Km and Vmax of Component II were 80 µM and 0.23 nmoles/min/10^6 RBC. In the control group the ^{App}Kcat and ^{App}Kcat/Km value were 10.7 x 10^5 and 3.75x10^6. In the diabetic group these values decreased respectively almost by 50 and 60 %. With ATP as the substrate, component I of diabetic group showed the significant decrease in ^{App}Kcat value (6.6 against 9.4). However, the ^{App}Kcat/Km was increased by 40%.

Table 7. Kinetic properties of erythrocyte phosphofructokinase in type 2 diabetes

		Component-I		Component-II	
Substrate	Parameter	Control (n=12)	Diabetic (n=40)	Control (n=12)	Diabetic (n=40)
F-6-P	K_m (µM)	290 ± 10	370 ± 10***	-	-
	V_{max}	0.27 ± 0.01	0.14 ± 0.01***	-	-
	$K_{cat}\times10^5$	10.7 ± 0.05	5.2 ± 0.03***	-	-
	$^{App}K_{cat}/K_m \times10^6$	3.75 ± 0.22	1.45 ± 0.09***	-	-
ATP	K_m (µM)	50 ± 8	20 ± 7*	-	80 ± 0.03
	V_{max}	0.24 ± 0.02	0.17 ± 0.01**	-	0.23 ± 0.01
	$K_{cat}\times10^5$	9.4 ± 0.07	6.6 ± 0.04***	-	8.7 ± 0.05
	$^{App}K_{cat}/K_m \times10^6$	23.82 ± 4.07	38.32 ± 2.99*	-	12.28 ± 1.19

The results are given as mean ± SEM of number of observations indicated in parentheses.
*, p <0.05; **, p <0.001; ***, p <0.0001.

The data from Table 8 show that in the control group, one molecule of F-6-P was bound to enzyme till F-6-P concentration reached 1.81 mM; beyond this concentration two molecules of F-6-P were bound. As against this, in the diabetic group, beyond the 2.0 mM F-6-P concentration three molecules of F-6-P were bound to enzyme. In the case of ATP, in the control group one can note that after 275 µM of ATP, two molecules of ATP were bound to the enzyme. Further in diabetic group the pattern was comparable to the controls.

Table 8: Hill plot analysis of erythrocyte phosphofructokinase in type 2 diabetes

Substrate	Subject	HiII Coefficient		Transition Concentration (µm)
		n_1	n_2	
F6P	Control (n=12)	1.07 ± 0.01	2.34 ± 0.01	1807.6 ± 46.08
	Diabetic (n=40)	1.08 ± 0.01	3.18 ± 0.17	1987.5 ± 46.04*
ATP	Control (n=12)	1.16 ± 0.02	2.56 ± 0.13	275.0 ± 13.0
	Diabetic (n=40)	0.73 ± 0.02	3.10 ± 0.12	310.0 ± 10.0 NS

The results are given as mean ± SEM of number of observations indicated in parentheses. *, p <0.05, NS, Not significant.

Conclusion: The substrate saturation kinetics and substrate binding characteristics of erythrocyte hexokinase and phosphofructokinase were significantly altered in type 2 diabetes. Decreased phosphofructokinase activity could lead to impairment of glycolysis and ATP synthesis. Inadequate/disproportionate spectrin-ATP interaction may one of the underlying cause of loss of deformability of erythrocyte membrane. Following manuscripts communicated:
Bhise SS, Rao JR, Hegde MV, Katyare SS. Compositional alterations in erythrocyte membranes in Type II Diabetes. Ind J Exp Biol. 2019.
Bhise SS, Rao JR, Hegde MV, Katyare SS. Type 2 diabetes differentially affects the substrate saturation kinetics attributes of erythrocytes hexokinase and phosphofructokinase. FEBS Letters. 2019.

5. **Title:** Exploring the Antimetastatic Breast Cancer Potential of the Flax Lignans (**Project ID:** CINHD/18/2/I/P)

Funding: BVDU, Pune; **Guide:** Prof. Dr. Shivajirao S. Kadam; **Co-Guide:** Prof. M. V. Hegde, **Ph.D. student:** Mr. Aniket V. Mali; **Duration of the project:** Nov 2012 – May 2019
Background: The aim of the present study was to investigate molecular and cellular mechanisms to establish the therapeutic value of Enterolactone (EL), a mammalian lignan derived from the flax lignan as a potential anti-cancer and anti-metastatic molecule in triple negative breast cancer (TNBC). This project has been successfully completed and closed as all the objectives of the project are achieved.
Work done: All the university requirements for the 2nd Ph.D. presentation were fulfilled and submitted the progress report of the same, after successful presentation of the work in front of internal evaluation committee. All the university requirements for the 3rd Ph.D. presentation were fulfilled and submitted the progress report of the same, after successful presentation of the work in front of internal evaluation committee. At the time of 3rd Ph.D. presentation, the first draft of PhD thesis was presented and was approved by the internal evaluation committee for the submission. The final draft of Ph.D. thesis was submitted on 6th Dec 2018 to the PhD section of Bharati Vidyapeeth (Deemed to be University) under the faculty of Pharmaceutical Sciences.
The final Ph.D. viva was successfully defended on 13th May 2019 and Ph.D. completion notification was received on 20th May 2019.

Conclusion: In this project we have concluded that Enterolactone (EL) a mammalian lignan derived from dietary lignans, exerts its antimetastatic breast cancer activity by suppressing invasion, migration, colonization in-vitro; inhibiting uPA/Plasmin/MMPs mediated ECM remodeling and reverting EMT via modulation of ERK-NFκB-Snail signaling pathway in triple negative MDA-MB-231 breast cancer cells. These findings suggest the possible role of EL in targeting the CSCs and affecting cancer initiation, metastasis and relapse. Along with our work, research works of others also project EL as a novel candidate to be investigated as an alternative targeted therapy for TNBC.

6. **Title:** Developing Omega-3 Edible Oil Blends and Evaluating Their Effects and Safety in Pre-clinical Studies. (**Project ID:** CINHD/18/3/I/P)
Duration: Registered in August 2018; **Guide:** Dr. Anand A. Zanwar; **Co-Guide:** Prof. M. V. Hegde, **Ph.D. student:** Mrs. Asavari A. Joshi

Background: The pre-course Ph.D. work was successfully completed. The Review of literature, aims, objectives and methodology was presented which was approved by the review committee. Flax seed oil was used as omega-3 fatty acid source for the blending studies. Two commonly used oils selected for the blending purpose are Palm olein and groundnut oil.
Work done: Palm olein (P) and Groundnut oil have been selected for flaxseed oil (FSO) blending FSO blends with P containing 20, 10 and 5% FSO were prepared and referred as P20, P10 and P5 respectively Nutritive quality, oxidative stability and thermal stability has been analyzed Individual oils and their blends have been evaluated for their effect on cell viability and inflammatory markers in THP1 cell line
Results:
Physico-chemical characterization of Palm olein oil blends has been done
Physico-chemical characterization of the individual oils and their blends was carried out as per AOCS guidelines or published methodologies.

Table 9. Evaluation of nutritive quality of blends by fatty acid analysis

	FSO	P	P5	P10	P20
PA	6.61±0.08 [e]	41.36±0.16 [a]	39.17±0.08 [b]	36.73±0.33 [c]	33.55±0.05 [d]
SA	6.59±0.07 [b]	3.91±0.06 [a]	3.44±0.68 [a]	4.20±0.05 [a]	3.83±0.22 [a]
OA	21.61±0.01 [e]	43.83±0.01 [a]	42.78±0.25 [f]	41.31±0.04 [c]	38.83±0.07 [c]
LA	14.47±0.10 [e]	10.89±0.11 [a]	11.59±0.81 [a, f]	11.39±0.12 [a, f]	11.78±0.04 [f]
ALA	50.72±0.23 [e]	-	3.01±0.2 [b]	6.37±0.19 [c]	12.00±0.16 [d]
LA/ALA	0.29±0.00 [e, d]	-	3.85±0.02 [b]	1.79±0.03 [c]	0.98±0.01 [d, g]

Table 9: Evaluation of nutritive quality of blends by fatty acid analysis by GC-FID. The FA composition of the oils and their blends was determined by GC-FID by the method described by Ichihara and Fukubayashi with some modifications. Two Way ANOVA and Bonferroni Post test was applied to determine statistical significance between and among different FAs present in the oils and blends. Different letters in a row (a, b, c, d and e: $p<0.001$, f: $p<0.01$ and g: $p<0.05$ P10 vs P20) represent statistically significant difference between the means.

Table 10: Various parameters assessed for evaluating stability of blends

Oil	Parameters (immediately after blend preparation)			
	AV (mg KOH/ g oil)	% FFA (as oleic acid)	PV (mill.eq. O_2/ kg oil)	Smoke Point (^{0}C)
FSO	0.48±0.09	0.2±0.01	0.4±0.03	103±1.41
P	0.65±0.1	0.26±0.03	1.12±0.1	212.5±3.53

P20	0.69±0.07	0.26±0.02	2.0±0.3	203.5±2.12
P10	0.65±0.05	0.26±0.03	1.37±0.22	203±1.41
P5	0.63±0.02	0.26±0.01	1.12±0.13	203.5±2.12

Table 10: Various parameters assessed for evaluating stability of blends. Acid Value, %FFA, Peroxide Value and Smoke point were determined either by following AOCS methods or published methodology. Values for AV, %FFA and PV were in the range given by Codex Guidelines. Similarly, the Smoking points of the blends were well above the temperatures achieved during the domestic cooking.

Effect of oils and blends on cell viability

Effect of blends on cell viability was evaluated in THP1 cells at 50, 100 and 250µg/ml for 24, 48 and 72 h by MTT assay. Data for 250µg/ml of oils and blends for all the three time points is presented here.

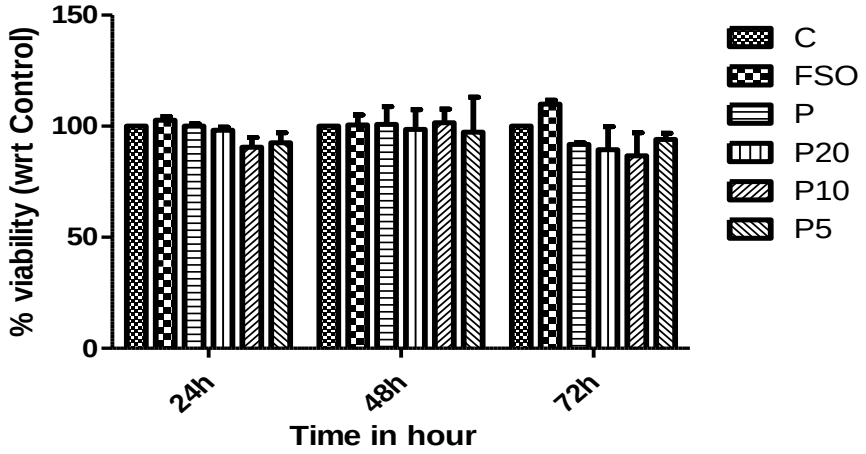


Fig. 10: Viability of THP1 cells treated with individual and blended oils: THP1 cells were treated with individual and blended oils (250µg/ml) for 24, 48 and 72 h. At the end of incubation periods, MTT assay was done to determine viability. Data is represented as % viability wrt Control from two different experiments conducted in replicates.

Effect of oils and blends on inflammatory markers

Effect of blends on inflammatory markers (i.e. TNFα and IL-6) was evaluated in THP1 cells using commercially available ELISA kits.

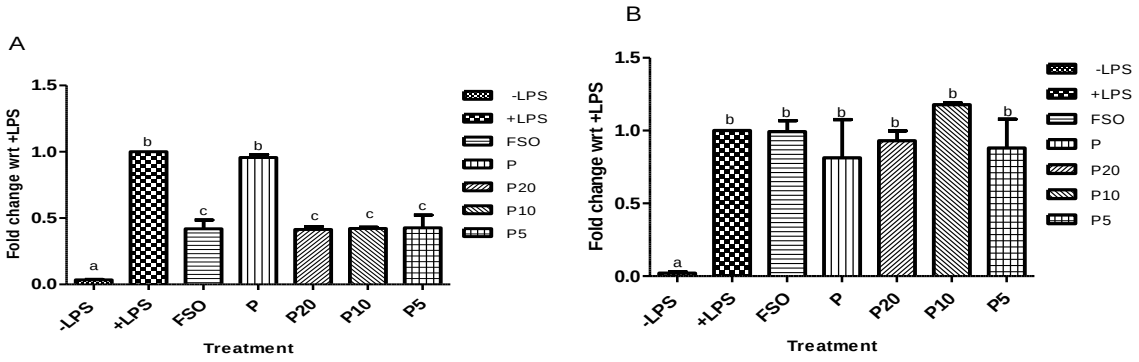


Fig. 11. Effects of oils and blends on the production of TNFα (A) and IL-6 (B) in THP-1 cells. THP-1 cells were pretreated with individual oils or blends (250µg/ml) for 48 h in RPMI-1640 medium followed by co-incubation with LPS (25ng/ml) for 24 h. Data are presented as fold change wrt –LPS from two independent experiments. Bars labeled with different letters are statistically significant ($p < 0.01$).

The palm olein oil blends containing 20, 10 and 5% FSO were prepared. Their physico-chemical characteristics were within the recommended range (Table 9-10). The cell viability data indicated that at 250 µg/ml, upto 72 h, these blends did not affect viability of the THP-1 cells (Fig. 10). Effect on inflammatory parameters showed that blending FSO in the palm olein did down regulate TNF-α, master regulator of inflammation (Fig.11).

Conclusion: Physico-chemical characteristics of blends showed that the blends can be as cooking oils. The fatty acid analysis showed that FSO and P blends had lower omega-6: omega-3 ratio and these blends have capacity to lower the inflammation (TNF-α).

5. Title: Evaluation of wound healing activity of omega-3-fatty acid in combination with silver sulfadiazine in rats Project ID: INHD/16/3/I
Funding: BVDU, Pune; **Investigators/ Co-Is / Co-PIs:** Dr. Anand Zanwar, Dr. M.V. Hegde
Collaboration: Dr. Shanta Modak, Dept. of Surgery, Columbia University, New York, USA
Animal Ethics Committee approval: **BVDUMC/l880/2018/002/009;** Duration: **March 2016-2019** March

Background: Last year, it was observed that topical application of silver sulfadiazine in combination with linseed oil (omega-3 fatty acid) showed better wound healing activity than that of silver sulfadiazine alone. Further preliminary results also indicated gel formulation offers more advantage than that of cream formulation and stability of linseed oil was better in case of gel than that of cream formulation. Considering this year we have modified our formulation from cream to gel form and viscosity of gel is also improved, in keeping the similar composition of active ingredients in gel. All the formulations were developed by Dr. Shanta Modak at Dept. of Surgery, Columbia University, New York, USA.

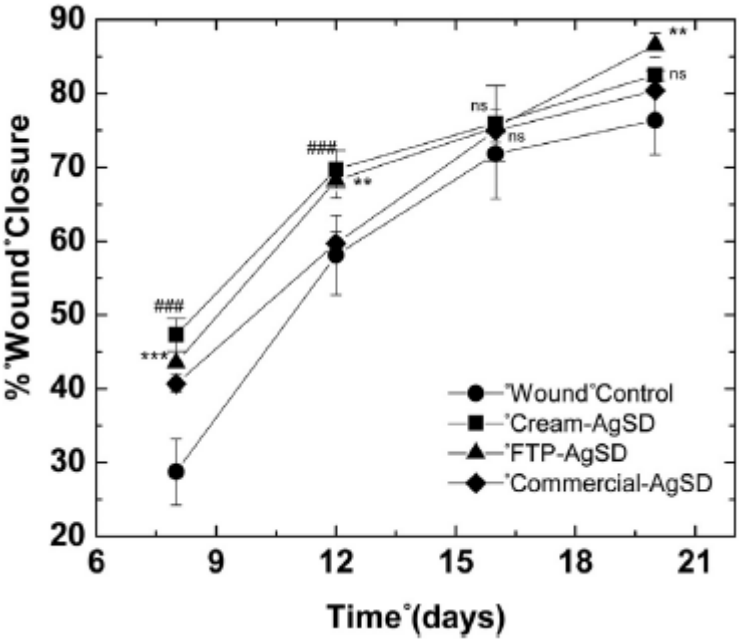
Objective: The objective of study was to evaluate the comparative wound healing potential of topical gel and cream containing silver sulfadiazine in combination with omega-3-fatty acids in excision wound model in laboratory rats.

Work done: Excision wound model: excision wounds were used for the study of rate of contraction of wound. Animals were anaesthetized with ketamine (80mg/kg, i.p), shaved and an impression of size 500 mm^2 and 2 mm depth was made on the back of neck. Excision wounds were made by cutting out layer of skin from the shaven area. Hemostasis was achieved by blotting the wound with cotton swab soaked in normal saline. The entire wound is left open. The progressive changes in wound area were measured on predetermined days i.e., day 8, 12, 16 and 20 post-treatment. Animals were divided in following four groups: Grouping: Wound control (no treatment), Silversulfadiazine + omega-3-fatty acids cream (Cream- AgSD),

Silversulfadiazine + omega-3-fatty acids gel (FTP-AgSD), Standard group-Silver sulfadiazine (Commercial-AgSD).

Results: The results show that FTP-AgSD gel shows similar or better wound healing properties to Cream- AgSD and Commercial-AgSD groups. Furthermore, FTP-AgSD aids in the wound healing process to heal and contract the wound faster, when compared to control group and Commercial-AgSD groups on day 8 ($p < 0.001$), day 16 ($p < 0.01$) and day 20 ($p < 0.05$). Further, FTP-AgSD showed significant improvement on day 20 ($p < 0.05$) as compared to control group. Similar wound contraction was noted in Cream-AgSD and Commercial-AgSD (Fig 7).

Figure 7: Wound contraction comparison on Day 8, 12, 16 and 20 post treatment



Conclusion: FTP-AgSD formulation was found to be non-toxic, and comparable with commercial AgSD with respect to wound healing efficacy. This project is completed and manuscript entitled “Smart polymer enhances the efficacy of topical antimicrobial agents”, communicated to Burns journal is accepted for publication and right now in press.

Budget (April 2018 to March 2019)

Budget Summary: (Total Amount Recd from Various Agencies: Rs.1129.73 Lakhs; Total Expenditure: Rs. 480.02 Lakhs)

Extramural Grants: (Total No: of Ongoing Grants: 25)

S. No	Funding Agency	Name of the Project	Amount Sanctioned (INR) In Lakhs	Amount Received (INR) In Lakhs	Expenditure (INR) In Lakhs
1	DBT-BIRAC	Establishment of National Centre for Immunogenicity Testing, NCIT to evaluate vaccines in clinical trials	16 crore	625.00	--
2	Department of Biotechnology, Govt. of India	DBT - Helti Project	Total Sanctioned Amount 743.44 IRSHA Share 13.50	10.50	6.80
3	Indian Council of Medical Research, Govt. of India	ICMR - Centre for Advance Research	681.53	140.19	141.82
4	ICMR and Serum Institute of India	Establishment of a novel Electronic Surveillance System for dengue in Pune: an initiative for Smart Cities Mission	400.10	113.19	117.28
5	Regulation of hematopoietic stem cell function in obesity by mitochondrial metabolism	DBT - Wellcome India Alliance	343.84	39.01	26.29
6	Dept. of Biotechnology,	DBT Placenta Project	Total Sanctioned		52.26

	Govt. of India		Amount 170.00 IRSHA Share 68.50		
7	Wellcome-DBT Indian Alliance	Development of potent adjuvanted respiratory syncytial virus vaccine for mucosal delivery	168.93	8.71	0.50
8	GSK	Prevalence of titers of Measles, Mumps, Rubella, Varicella antibodies in Indian infants and toddlers: A pilot study	86.66	20.00	24.95
9	EMR AYUSH (CCRUM)	Evaluating the anticancer activity and mechanism of action of Unani formulation Habbe Musaffi Khoon against cervical cancer	57.56	25.30	8.12
10	DST- Satyam	Effect of Yoga intervention on skeletal muscle linked glucose homeostasis in pre diabetic individuals	46.74	15.93	0.35
11	ICAR-AICRP-Linseed Value Addition Centre	ICAR	44.64	28.47	17.18
12	EMR AYUSH (CCRH)	Evaluating the anticancer activity of homeopathic preparation of Linum usitatissimum in breast cancer	42.02	25.92	8.92
13	Dept. of Science and Technology, Gove. Of India	DST - Preterm Project	40.48		8.58
14	Evaluation of efficacy of novel stabilized omega-3-fatty acid and	DST SERB	40.36	4.00	8.42

	antioxidants formulation for the prevention and treatment of metabolic syndrome				
15	ICMR-DHR	Immune response of Indian preterm infants to pentavalent vaccine	34.22	7.00	12.24
16	DST SERB	Evaluating the effect of Alpha linolenic acid (ALA), an omega 3 fatty acid, on modulation of epigenetic markers in cervical cancer cell lines.	33.16	11.05	5.61
17	DST WOS A	Comparing vaginal microflora diversity between healthy and cervical cancer women for identifying isolates having probiotic and anticancer potential	32.22	10.76	7.09
18	DST-SERB	Evaluation of different adjuvants for development of potent chikungunya vaccine	32.22	13.49	10.85
19	Evaluation of cardio protective activity of an herbal formulation in rat model of isoprenaline induced myocardial infraction	Dabur Research & Development Center, Dabur India Ltd.	5.34	4.89	2.14
20	CDC, USA and Bharati Vidyapeeth	Norovirus surveillance among children with acute gastroenteritis in Pune, India	-	5.00	1.65
21	DBT-BioCARe	Platelet derived exosomes and their role	46.39	-	-

		in endothelial dysfunction in dengue infection			
22	DBT-BioCARe	Epigenetic regulation of placental peroxisome proliferator activated receptor (PPAR) in women delivering low birth weight babies	35.50	-	-
23	EMR AYUSH (CCRH)	Evaluating the anticancer activity of different higher homeopathic potencies (200C, 1M, 10M, 50M, CM) of Terminalia chebula (TC) in breast cancer cell lines and analyzing the best potency for activity against in vivo breast cancer model (Completed in 2019)	42. 98	8.76 (Carry forward received) 8102/-	8.83
24	Evaluation of Triphala and Trimad for their effects on adipocytes biology and lipid metabolism	Ministry of AYUSH (Completed in Jan, 2019)	28.32	6.44	0.60
25	Department of Science and Technology, Govt. of India	INNO INDIGO Project	70.42	5.00	3.53
24	Dept. of Biotechnology, Govt. of India	DBT Children Follow up (Completed in June, 2018)	49.80		2.91
25	Indian Council of Agriculture Research, Govt. of India	ICAR - NASF Project (Completed in June, 2018)	46.44	1.12	1.35
27		Pharmanza Project (Completed in Dec, 2016)	8.97	-	1.39

28		Baidyanath Obesity (Completed in Dec 2016) study	2.89		0.060
29		RUSA PEG Study Project (Completed in Oct, 2017)	0.65		0.30

Student Fellowships: (Total Amount Received: Rs.32.36 Lakhs; Total Expenditure: Rs.27.30 Lakhs)

Sr. No	Funding Agency	Name of the Student	Amount Sanctioned (INR)	Amount Received (INR)	Expenditure
1	Indian Council of Medical Research, Govt. of India, New Delhi.	Ms. Amrita Khaire (ICMR – RA)	17.44	4.84	3.06
2	Department of Science and Technology, Govt. of India	Ms. Akriti Sahay (DST Inspire-SRF)	18.92	0.42	0.42
3	Department of Science and Technology, Govt. of India	Ms. Alka Rani (DST Inspire-SRF)	17.04	2.31	2.31
4	Department of Science and Technology, Govt. of India	Ms. Shruti Jawale (DST Inspire- SRF)	21.48	4.36	4.36
5	University Grant Commission, New Delhi.	Fellowship Ms. Anindita Nandi (UGC- SRF)	21.70	0.30	0.12
6	Department of Science and Technology, Govt. of India	Ms. Vaishali Kasture (DST Inspire- SRF)	21.90	4.29	4.26
7	Department of Biotechnology, Govt. of India, New Delhi	Amol Chaudhari (DBT JRF)	7.51	7.51	7.51
8	Indian Council of Medical Research, Govt. of India, New Delhi.	Ms. Anjali Jadhav (ICMR – SRF)		3.80	2.15
9	Council of Scientific & Industrial Research,	Ms. Juhi Nema (CSIR- JRF)	21.90	0.89	0.84

	Govt. of India, New Delhi.				
10	Council of Scientific & Industrial Research, Govt. of India, New Delhi.	Ms. Kinjal Dave (CSIR- JRF)	21.90	0.89	0.83
11	Department of Biotechnology, Govt. of India, New Delhi	Akanksha Mahajan (DBT JRF)	1.94	-------	-------
12	Department of Science and Technology, Govt. of India	Prajakta Biradar (DST Inspire-JRF)	Sanctioned amount letter is not received yet	-------	-------
13	Department of Science and Technology, Govt. of India	Rama Rajadnya (DST Inspire-JRF)	Sanctioned amount letter is not received yet	-------	-------
14	IASTAM-India (October-2018)	Shital Giramkar	0.50	0.20	0.68
15	Sakal India Foundation (March 2019)	Shital Giramkar	0.40	0.20	0.03
16	Council of Scientific & Industrial Research, Govt. of India, New Delhi.	Manoj M. Khavate (CSIR-JRF)	1.62	1.62	
17	Indian Council of Medical Research, Govt. of India, New Delhi.	Ms. Mrunal Gosavi (ICMR-SRF)	16.22	-	-
18	Department of Science and Technology, Govt. of India, New Delhi	Travel Grant-Ms. Deepali Sundrani		0.73	0.73

Total Publications: (Research Articles: 16; Book Chapters:01; Patent Application:03)
Research Articles

S.no	List of Publication	Impact	Scopus	Web of	Pubmed

		Factor		Science	
1	Kapil U, Joshi S. Markers of Maternal and Neonatal Cobalamin Status and Risk Assessment of Neurodevelopmental Disorders in Infants. Indian J Pediatr. 2018 Jul;85(7):491-492. doi: 10.1007/s12098-018-2683-3. Epub 2018 May 3. Review. No abstract available.	**1.508**	**N**	**N**	**Y**
2	Kemse N, Kale A, Chavan-Gautam P, Joshi S. Increased intake of vitamin B12, folate, and omega-3 fatty acids to improve cognitive performance in offspring born to rats with induced hypertension during pregnancy.Food Funct. 2018 Jul 17;9(7):3872-3883. doi: 10.1039/c8fo00467f.	**4.171**	**Y**	**N**	**Y**
3	Mishra AC, Arankalle VA, Gadhave SA, Mahadik PH, Shrivastava S, Bhutkar M, Vaidya VM. Stratified sero-prevalence revealed overall high disease burden of dengue but suboptimal immunity in younger age groups in Pune, India. PLoS Negl Trop Dis. 2018 Aug 6;12(8):e0006657. doi: 10.1371/journal.pntd.0006657. eCollection 2018 Aug.	**3.885**	**Y**	**Y**	**Y**
4	Sahay AS, Jadhav AT, Sundrani DP, Wagh GN, Mehendale SS, Joshi SR. Matrix metalloproteinases-2 (MMP-2) and matrix metalloproteinases -9 (MMP-9) are differentially expressed in different regions of normal and preeclampsia placentae. J Cell Biochem. 2018 Aug;119(8):6657-6664. doi:	**3.448**	**Y**	**Y**	**Y**

	10.1002/jcb.26849. Epub 2018 Apr 17. PMID:29665148				
5	Kasture VV, Sundrani DP, Joshi SR. Maternal one carbon metabolism through increased oxidative stress and disturbed angiogenesis can influence placental apoptosis in preeclampsia. Life Sci. 2018 Aug 1;206:61-69. doi: 10.1016/j.lfs.2018.05.029. Epub 2018 May 14. Review.PMID:29772225	**3.647**	**Y**	**Y**	**Y**
6	Kamble, A., Shetty, V., Shendokar, S.M., Chavan, S.S. and Kaul-Ghanekar, R. Synthesis, Characterization and Antibacterial Activity of Ciprofloxacin Loaded Electrospun Gelatin Nanofibers. Journal of Bionanoscience, 2018 Oct; 12(5), pp.715-720.	-	**Y**	**N**	**N**
7	Aphale, S., Pandita, S., Raina, P., Mishra, J.N. and Kaul-Ghanekar, R. Phytochemical standardization of panchavalkala: An ayurvedic formulation and evaluation of its anticancer activity in cervical cancer cell lines. Pharmacognosy Magazine, 2018 Nov; 14(58), p.554.	**1.31**	**N**	**N**	**N**
8	Kulkarni R, Tiraki D, Wani D, Mishra AC, Arankalle VA. Risk of transfusion-associated dengue: screening of blood donors from Pune, western India. Transfusion. 2019 Feb;59(2):458-462. doi: 10.1111/trf.15007. Epub 2018 Nov 10.	**2.8**	**N**	**Y**	**Y**

9	Jawale S, Joshi S, Kale A. Maternal dairy fat diet does not influence neurotrophin levels and cognitive performance in the rat offspring at adult age. Int J Dev Neurosci. 2018 Dec;71:18-29. doi: 10.1016/j.ijdevneu.2018.08.002. Epub 2018 Aug 12.	**2.025**	**Y**	**N**	**Y**
10	Deepak M Kasote, Minal V Pawar, Shridevi S Gundu, Riya Bhatia, Vinod S. Nandre, Suresh D Jagtap, Swapnil G Mahajan & Mohan V Kulkarni. Chemical profiling, antioxidant, and antimicrobial activities of Indian stingless bees propolis samples. Journal of Apicultural Research. 2019 March; 58(4): 617-625.	-	**Y**	**Y**	**N**
11	Malshe N, Palkar S, Kulkarni R, Lalwani S, Mishra AC, Arankalle V. Early disappearance of maternal anti-measles, mumps, rubella, and varicella antibodies in Indian infants. Vaccine. 2019 Mar 7;37(11):1443-1448. doi: 10.1016/j.vaccine.2019.01.043. Epub 2019 Feb 11.	**3.269**	**Y**	**Y**	**Y**
12	Kasture V, Dalvi S, Swamy M, Kale A, Joshi S. Omega-3 fatty acids differentially influences embryotoxicity in subtypes of preeclampsia. Clin Exp Hypertens. 2019 Apr 9:1-8. doi: 10.1080/10641963.2019.1601208. [Epub ahead of print]	**1.234**	**Y**	**Y**	**Y**
13	Yadav H, Dangat K, Randhir K, Khaire-Ghadge A, Mehendale S,	**2.433**	**Y**	**N**	**Y**

	Joshi S. Higher Maternal Plasma Folate, Vitamin B12 and Homocysteine Levels in Women with Preeclampsia. J Hum Hypertens. 2019 May;33(5):393-399.				
14	Gupte PA, Giramkar SA, Harke SM, Kulkarni SK, Deshmukh AP, Hingorani LL, Mahajan MP, Bhalerao SS. 'Evaluation of the efficacy and safety of Capsule Longvida® Optimized Curcumin (solid lipid curcumin particles) in knee osteoarthritis: a pilot clinical study'. J Inflamm Res. 2019 June; 12:145–152	**4.953**	**Y**	**Y**	**Y**
15	Mali AV, Padhye SB, Anant S, Hegde MV, Kadam SS. Anticancer and antimetastatic potential of enterolactone: Clinical, preclinical and mechanistic perspectives. Eur J Pharmacol. 2019 Jun 5;852:107-124. IF: 3.170.	**3.170**	**Y**	**Y**	**Y**
16	Arankalle V, Tiraki D, Kulkarni R, Palkar S, Malshe N, Lalwani S, Mishra A. Age-stratified anti-HAV positivity in Pune, India after two decades: Has voluntary vaccination impacted overall exposure to HAV? J Viral Hepat. 2019 Jun;26(6):757-760. doi: 10.1111/jvh.13074. Epub 2019 Mar 5.	**3.561**	**Y**	**N**	**Y**

Book Chapters:

Panse ML, Phalke SD. Omega-3 Beverages. In. Value-Added Ingredients and Enrichments of Beverages. Academic Press, Eds: Alexandru Mihai Grumezescu, Alina Maria Holban, 2019 June, 353-382, ISBN 9780128166871. https://doi.org/10.1016/B978-0-12-816687-1.00011-4.

Papers presented in International Conferences/Seminars/Workshops: (Total No: 20)

1. Akriti Sahay, Deepali Sundrani, Girija Wagh, Savita Mehendale, Sadhana Joshi. Differential expression of matrix metalloproteinases-2 (MMP-2) and matrix metalloproteinases-9 (MMP-9) in different regions of normal and preeclampsia placentae at the 21th Annual SNEHA-MRC International workshop on Developmental Origins of Health and Diseases (DOHaD), Pune, KEM hospital, 8th – 10th February, 2019
2. Shweta Madiwale, Karuna Randhir, Nisha Wadhwani, Hemlata Pisal, Kamini Dangat, Shridevi Gundu, Prachi Joshi, Girija Wagh, Sanjay Gupte, Caroline Fall, Sadhana Joshi. Socioeconomic differences in dietary intake patterns of women in early pregnancy at the 21th Annual SNEHA-MRC International workshop on Developmental Origins of Health and Diseases (DOHaD), Pune, KEM hospital, 8 th – 10 th February, 2019
3. Anindita A. Nandi, Nisha S. Wadhwani, Sadhana R. Joshi "Maternal Vitamin D Deficiency Increases the Thromboxane/Prostacyclin Ratio through Alterations in the One Carbon Cycle in Wistar Rats" at the 21th Annual SNEHA-MRC International workshop on Developmental Origins of Health and Diseases (DOHaD), Pune, KEM hospital, 8 th – 10 th February, 2019
4. Vaishali Kasture, Deepali Sundrani, Surabhi Dalvi, Mayur Swamy, Anvita Kale, Sadhana Joshi. "Maternal Omega-3 Fatty Acids improve Placental Angiogenesis in Late Onset but not Early Onset Preeclampsia" at 21st Annual SNEHA-MRC International Workshop, Venue- KEM hospital, Pune, India Date- 8-10 FEB 2019
5. Dave Kinjal. Assessing the effect of RUTF (Ready-to-use therapeutic food) on the body composition parameters of severely malnourished children. International Course in Nutrition Research Methods [Bangalore Boston Nutrition Collaborative (BBNC)], 7th- 18th January 2019 at St. Johns Research Institute , Bangalore, India
6. Anindita Nandi, Nisha Wadhwani, Sadhana Joshi (2018) "Vitamin D deficiency influences fatty acid metabolism" at 50th Annual International conference of Nutrition Society of India"India's Transition from Food Security to Nutrition Security"Venue- National Institute of Nutrition, Hyderabad, Telangana, India, Date- 15- 17 November 2018. (Young Scientist Award paper)
7. Vaishali Kasture, Surabhi Dalvi, Mayur Swamy, Anvita Kale, Sadhana Joshi (2018) "Omega-3 fatty acids differentially influences embryotoxicity in Subtypes of preeclampsia" at at 50th Annual International Conference of Nutrition Society of India held at NIN, Hyderabad on 15th - 17th November 2018. (Young Scientist Award paper)

8. Juhi Nema, Deepali Sundrani, Karuna Randhir, Nisha Kemse, Shridevi Gundu, Sanjay Gupta, Sadhana Joshi. Vitamin D status in pregnancy and its association with neonatal vitamin D: A longitudinal Study at the 50th International Conference of NSI organized at NIN, Hyderabad on 15th -17th 2018. (Oral Presentation)
9. Deepali Sundrani, Kamini Dangat, Hemlata Pisal, Anupam Poddar, Sakshi Selukar, Girija Wagh, Savita Mehendale, Sadhana Joshi. Maternal long chain polyunsaturated fatty acid status in early pregnancy and placental dimensions at 50th Annual International Conference of Nutrition Society of India (NSI), at National Institute of Nutrition, Hyderabad, Telangana., 15th-17th November, 2018. (Oral Presentation)
10. Shruti Jawale, Sadhana Joshi, Anvita Kale (2018) "Short And Long Term Effects Of Maternal Butter Consumption On Adult Wistar Rat Offspring Cardiometabolic And Neurodevelopmental Health" 50th Annual International Conference of Nutrition Society of India held at Hyderabad, 15th -17th November, 2018 (Poster Presentation Experimental Nutrition).
11. Anjali Jadhav, Amrita Khaire, Karuna Randhir, Sagar Bhosale, Shridevi Gundu, Prachi Joshi , Girija Wagh, Sanjay Gupte, Sadhana Joshi. Women with higher bmi in early pregnancy have lower long chain polyunsaturated fatty acid levels at 50th Annual International Conference of Nutrition Society of India (NSI), at National Institute of Nutrition, Hyderabad, Telangana, 15th-17th November, 2018. (Poster Presentation)
12. Kinjal Dave, Nisha Wadhwani, Yasmin Aktar, Aditi Mane, Girija Wagh, Savita Mehendale, Sanjay Gupte, Sadhana Joshi. Maternal micronutrient status in erly pregnancy in two different socioeconomic groups at 50th Annual International Conference of Nutrition Society of India (NSI), at National Institute of Nutrition, Hyderabad, Telangana., 15th-17th November, 2018. (Poster Presentation)
13. Amrita Khaire, Hemlata Pisal, Kamini Dangat, Karuna Randhir, Savita Mehendale, Sadhana Joshi "Micronutrient levels in women with preeclampsia and their association with birth outcome" at 50th Annual International Conference of Nutrition Society of India held at NIN, Hyderabad on 15th - 17th November 2018.
14. Oral presentation on "Association of inflammatory and endocrinological markers with body mass index (BMI) in PCOS patients" at 3rd International Diabetes Summit-2019 arranged by Chellaram Diabetes Institute, Pune on 8^{th} - 10^{th} March, 2019.
15. Oral presentation by Ms. Shama R. Aphale on " Phytochemical identification and evaluation of anticancer activity of an Ayurvedic formulation Panchvalkala in cervical cancer cell lines" at 'International Conference on Advances in Medical and Industrial Biotechnology 2019' held at Sathyabama Institute of Science and Technology (Deemed to be University), Chennai from 20th to 23rd March 2019.

16. Oral presentation by Ms. Varsha Shetty on 'Cinnamaldehyde loaded iron oxide nanoparticles exhibit anticancer activity in breast cancer cell lines' at International Conference on 'Advances in Medical and Industrial Biotechnology, 2019' held at 'Sathyabama Institute of Science and Technology (Deemed to be University), Chennai from 20th to 23rd March 2019.
17. Oral presentation by Apoorva Parimoo on 'Homoeopathic potencies of Terminalia chebula decrease the viability of breast cancer cell lines' at International Conference on 'Advances in Medical and Industrial Biotechnology, 2019' held at 'Sathyabama Institute of Science and Technology (Deemed to be University), Chennai from 20th to 23rd March 2019.
18. Poster presenatation by Dr. Anand Zanwar on "Development of micronutrient rich, stabilized vegetarian omega-3-fatty acid formulation for food fortification" at NSI- India's Transition from Food Security to Nutrition Security, 15 -17 November 2018 held at ICMR-NIN, Hyderabad.
19. Paper presentation by Anand Zanwar on " Blending of linseed oil to edible oil to attain healthier omega-6 to 3 ratio and omega-3 nutritional security" at XIVth Agricultural Science Congress-2019- Innovations for Agricultural Transformation" during 20-23rd February 2019, held at ICAR, New Delhi.
20. Paper presentation by Ms. S. S. Bhise on " Alterations In Kinetic Attributes of HK1 In Diabetic RBC And Membrane Deformability" at 3rd International Diabetes Summit 2019, Pune (9th March 2019) held at Chellaram Diabetes Institute, Pune

Papers Presented at National Conferences/Seminars/Workshops: (Total No: 6)

1. Oral presentation on effect of therapeutic course of Takra basti (enema with processed buttermilk) in obese individuals by Dr. Sarika Mane on 13th AIAAROCON, 2018 held at Aurangabad on 8th -9 th sep 2018
2. Oral presentation on Challenges in planning clinical trials- our experiences Presenter by Dr. Poonam Gupte on 13th AIAAROCON, 2018 held at Aurangabad on 8th -9 th sep 2018
3. Oral presentation on Association of obesity and cognitive function in young age adults: A proof-of- concept study by Shital Giramkar on 13th AIAAROCON, 2018 held at Aurangabad on 8th -9 th sep 2018
4. Oral presentation on study of oxidative stress & inflammation in obesity by Megha Salunke on 13th AIAAROCON, 2018 held at Aurangabad on 8th -9 th sep 2018.
5. Speaker (Dr. Anand Zanwar, Dr. P. B. Ghorpade) at Annual Group Meeting on Linseed, 10-12 August 2018 held at Birsa Agriculture University, Ranchi.
6. Delegate (Dr. Anand Zanwar) at workshop on "Sensory Evaluation of Foods", 19-20 Oct 2018 held at NAFARI Institute Pune

Patent Application:

S.No	Patent Title	Name of Innovators	Patent No.	Filling date	Current status
1	Coatings and methods for infection-resistant medical devices	Hegde MV, **Zanwar AA**, Dongre S, Kadam SS, Modak SM, Ghosh AK, Silva SD.	US Patent Application No. 62/333905, Int. Appl. No: PCT/US2017/031969. International Publication No. WO 2017/200818 A1	10/05/2016	Published on 09-05-2019
2	Polymer films with antimicrobial agents	Modak SM, De Silva CC, Ghosh AK, **Zanwar AA**, Hegde M.	International Patent Application No. PCT/US18/44247	27/07/2018	Filled
3	Formulation of edible oil	Zanwar AA, Hegde M.	Provisional Indian Patent Application Application No. 201921006187	16/02/2019	Filled

Awards and Honors:

Faculty				
Sr. No	**Academic Year**	**Name of the Faculty Member**	**Name of Award / Honor**	**Details of Award / Honor**
1	2018-19	Prof. M. V. Hegde	Organizing Committee member	International Conference on Breast Cancer 2018 held at Dubai UAE: Dec 03-04 2018
2	2018-19	Prof. M. V. Hegde	Faculty and chairperson	3rd International Diabetes Summit

				2019, held at Chellaram Diabetes Institute, Pune
3	2018-19	Prof. M. V. Hegde	Co-chairman	Conclave on Food and Nutritional Security organized by Indian Society of Agricultural Biochemists
4	2018-19	Dr. Sadhana Joshi	9th Dr. Rajammal P. Devadas Memorial Award and delivered the oration lecture during the National Institute of Nutrition Centenary year and 50th Annual International Conference of Nutrition Society of India.	This award was given for her outstanding contributions in the field of applied nutritional sciences as evidenced by peer review publications, projects handled and high academic pursuit.
5	2018-19	Dr. Sadhana Joshi	Board Member	Board Member for the Preterm Birth International Collaborative PREBIC Australasian Branch (China and Korea)
6	2018	Dr. Supriya Bhalerao	Secretary for World Ayurveda Congress held at Ahmadabad in Dec 18	-
7	2018-19	Dr. Anvita Kale	Best oral presentation in the Free Communication session	50th Annual International Conference of Nutrition Society of India held at

			(Experimental Nutrition) for the paper titled "Short and Long Term Effects of Maternal Butter Consumption on Adult Wistar Rat Offspring Cardiometabolic and Neurodevelopmental Health"	NIN, Hyderabad on 15th - 17th November 2018
8	2018-19	Dr. Anand Zanwar	Nominated as Principal Investigator	Linseed Biochemistry under ICAR-AICRP-Linseed program
9	2018-19	Dr. Anand Zanwar	Junior Researcher Travel Award	American Oil Chemist Society (AOCS) USA.
10	2018-2019	Ms. Kavita Shinde	Dr. A. P.J. Abdul Kalam Lifetime Achievement National Award', in the field of teaching, research and publication	International Institute for Social and Economic Reforms
Students				
1.	2018-19	Anindita Nandi	2nd prize for the "Best Poster Presentation" for the paper "Maternal Vitamin D Deficiency Increases the Thromboxane/Prostacyclin Ratio through Alterations in the One Carbon Cycle in Wistar Rats''	21st Annual SNEHA-MRC International Workshop on 10th Feb, 2019
2.	2018-19	Kinjal Dave	2nd position in	BBNC 2019 at St.

			Best Presentation for the project "Assessing The Effect Of RUTF on the body composition parameters of severely malnourished children"	John's research institute, Bangalore.
3.	2018-19	Vaishali Kasture	Young Scientist Award in Experimental Nutrition for the paper "Omega-3 fatty acids differentially influences embryotoxicity in Subtypes of preeclampsia"	50th Annual International Conference of Nutrition Society of India held at NIN, Hyderabad on 15th - 17th November 2018
4.	2018-19	Anindita Nandi	Young Scientist Award in Experimental Nutrition for the paper entitled "Vitamin D deficiency influences fatty acid metabolism"	50th Annual International Conference of Nutrition Society of India held at NIN, Hyderabad on 15th - 17th November 2018
5.	2018-19	Juhi Nema	Best oral presentation in the Free Communication session (Community Nutrition) for the paper titled "Vitamin D status in pregnancy and its association with neonatal vitamin D: A longitudinal	50th Annual International Conference of Nutrition Society of India held at NIN, Hyderabad on 15th - 17th November 2018

			study"	
6.	2018-19	Dr. Amrita Khaire	Best Poster presentation in the Free Communication session (Community Nutrition) for the paper titled "Micronutrient levels in women with preeclampsia and their association with birth outcome"	50th Annual International Conference of Nutrition Society of India held at NIN, Hyderabad on 15th - 17th November 2018
7.	2018-2019	Ms. Varsha Shetty	Certificate of Best Paper	Satyabama Institute of Science and Technology (Deemed to be University), Chennai at the International Conference on Advances in Medical and Industrial Biotechnology (ICAMIB)-2019.

Ph.D Degree Awarded:03

Sr. No	**Name of the Student**	**Name of the Guide**	**Topic**	**Month and Year of Award**
1	Ms. Akriti Srivastava	Dr. Sadhana Joshi	Regional Differences in Neurotrophin Regulation of Vascularization in Preeclamptic Placentae	Dec 2018
2.	Ms. Alka Rani	Dr. Preeti Chavan Gautam	Regional Differences in Fatty Acids Metabolism in Preeclamptic Placentae	May 2019
3.	Shubhangi	Dr. Aniket	Biochemical and molecular analysis	May 2019

	Harke	Kuvalekar	of adipose tissues in Type 2 diabetic human subjects	

Invited Talks by Faculty: 14

Sr. No	Academic Year	Name of the faculty	Topic
1	2018-19	Prof. M. V. Hegde	Key note address at International conference on Breast Cancer, December 3-4, 2018 at Dubai, UAE. Theme: Paving paths for discoveries for better diagnosis and awareness. Title of presentation: Distorted Fatty Acid Metabolism and Metabolic Syndrome
2	2018-19	Prof. M. V. Hegde	"Omega-3 Conclave", organized by Association of Physicians of India. Nagpur on 12th April 2019.
3	2018-19	Prof. M. V. Hegde	Speaker at IUFoST 2018-19th World Congress of Food Science and Technology Convention and Exhibition, Navi Mumbai. Title: "Linseed derived omega-3 products", during October 23-27, 2018.
4	2018-19	Prof. M. V. Hegde	Special talk at "Conclave on Food and Nutritional Security" during 25-27 Feb 2019", organized by Indian Society of Agricultural Biochemists, at Mahatma Pule Krishi Vidyapeeth Rahuri. Title of presentation: Unleashing the power of linseed for omega-3 Nutritional Security.
5	2018-19	Dr. Sadhana Joshi	Delivered a talk on the topic "Epigenetics and Developmental Origin of Health and Disease" at Symbiosis School of Biological Sciences 4th symposium on "Emerging Trends in Biomedical Sciences" 25th January, 2019.
6	2018-19	Dr. Sadhana Joshi	Delivered a talk on the topic "Maternal long chain polyunsaturated fatty acids and pregnancy complications" at NIN-ISSFAL symposium on Fats in maternal and child health nutrition (18th Sept, 2018).
7	2018-19	Dr. Sadhana Joshi	Delivered a talk on the topic "Role of Nutrition in Risk of Preeclampsia", at "New Delhi Birth Cohort Golden Jubilee Celebrations" conference on "Lessons from the Indian Birth Cohorts" (29th Sept, 2018).

8	2018-2019	Dr. Ruchika Kaul-Ghanekar	Exploring the Potential of Plant based Medicines in Cancer" at National Conference on Unani Medicine "Unani Medicine for Public Health" organized by Ministry of Ayush, VigyanBhavan, New Delhi, 11th-12th February, 2019.
9	2018-2019	Dr. Ruchika Kaul-Ghanekar	Mechanisms and mode of action of Ayurvedic formulations" under theme "Exploring evidence-based and comparative effectiveness research methods to evaluate Ayurvedic interventions for cancer" in Cancer Conclave of 8th World Ayurveda Congress and AROGYA 2018, 14-17 December 2018.
10	2018-19	Dr. Supriya Bhalerao	Developing methodology for evaluation of basic principles of Ayurveda at Workshop on Research Methodology organized on the occasion of 63rd Foundation day of Institute of Postgraduate Training & Research in Ayurveda, Jamnagar on 20th July 2018
11	2018-19	Dr, Supriya Bhalerao	Scope for cross talk between Ayurveda and Pharmacy at Bharati Vidyapeeth College of Pharmacy, Navi Mumbai on 12th January 2019
12	2018-19	Dr, Supriya Bhalerao	Ayurvedic understanding of metabolic diseases: learning and experiences at National Conference on Frontiers in Health Sciences" organized by the Institute of Medical Sciences, Banaras Hindu University (BHU), Varanasi on 12th March, 2019
13	2018-19	Dr. Ashwini Hinge	National Allied health Conference on Laboratory sciences, held at MMM college of health sciences, Chennai in 22-23 January 2019 on "Stem cell story: Focusing on hematopoietic stem cells"
14	2018-19	Dr. Ashwini Hinge	Invited speaker for scientific talk at Center for Stem Cell Research, Vellore on June 26, 2019 on "Mechanisms involved in regulation of hematopoietic stem cell function and fate decision".

Other Activities
Invited Lectures:02

Sr. No	Name of the Guest	Topic	Date
1	Dr. Vivek Patwardhan (Hirabai Cowasjee Jehangir Medical Research Institute)	Metabolic interrelation of Vitamin D with cholesterol and statins	27th March 2019
2	Mr. Satyam Kothari, ComplyWell Solutions, Gujarat	Training on GCLP practices and implementation	24/05/2019

Events Organized at IRSHA

Obesity Day:

On the occasion of the World Obesity Day, lectures were organized on "Pharmacological management of obesity" by Dr. Vijaya Pandit from Bharati Medical College and "Surgical management of obesity" by Dr. Kedar Patil, Bharati Hospital & Research Center, on 11th October 2018.

Ayurveda Day:

On the occasion of National Ayurveda Day, lecture was organized on "Prevention and Management of Obesity" by Dr. Mukund Sabnis from Aurangabad, on Saturday 3rd November 2018.

Yoga Day:

On the occasion of International Yoga Day, lecture was organized on "Introduction to Yoga Philosophy "by Dr. Mihir S. Hajarnavis from Tilak Ayurveda Mahavidyalaya, Pune, on 21st June 2019.

Review meeting for the performance of AICRP, Oilseeds (sunflower, safflower, castor) AICRP sesame & Niger and AICRP linseed of 14 ICAR-AICRP centres organized by CINHD , Chief Guest Dr. Manikrao Salunkhe Honorable VC, BV(DU), Pune held on 7-8 September, 2018 at IRSHA

Details of the key dignitaries visited during QRT meeting:

Sr. No	Date of Visit	Name of the Dignitaries	Occasion / Purpose of Visit	Any other remarks
01	7-8 September, 2018	Dr. Arvind Kumar, Vice Chancellor, Rani Laxmi Bai Central Agril. University, NH-75,Near Pahuj Dam, Gwalior Road, Jhansi,(UP) – 284003	ICAR-Quinquennial Review Team (QRT) meeting	Total 40 ICAR scientists from 14 AICRP centres participated in this meeting
02	7-8 September, 2018	Dr.P.K.Das Associate Dean, Institute of Agricultural Sciences, SOA		

		University Shampur, Bhubaneshwar-510 029, Odisha		
03	7-8 September, 2018	Dr. S.J. Kolte, Professor - Plant Pathology (Retd.), Paud Road, Kothrud, Pune – 411 038 (Maharashtra)		
04	7-8 September, 2018	Dr. P. Raghuram Professor (Ag. Economics) Department of Agri Business management SV Agricultural College Tirupati-517502, AP		
05	7-8 September, 2018	Dr. D. M. Hegde Former Director- ICAR- IIOR C-108, SMR Vinay Galaxy Hoody Junction, CTPL Road, White field, Mahadevapura, Bengaluru- 560048		
06	7-8 September, 2018	Dr. Lakshmi Prayaga, Principle Scientist, ICAR-IIOR, Hyderabad		
07	7-8 September, 2018	Dr. P. K. Singh Project Coordinator Linseed, Project Coordinating Unit Linseed, ICAR- Indian Institute of Pulses Research Kanpur		

Extension activities:

Extension activity for screening of anticancer activity of drugs is being provided to other institutions in which we have generated funds worth Rs.53,046.62/-.

Extension activities by Dr. P. B. Ghorpade (Emeritus professor):

One of the noteworthy extension activity if CINHD is the backward linkage with linseed group farmers in Vidhabha. It involves authentic seed production (PKV-NL-260) and its distribution to farmers and training of the farmers.

Seed Production:

Linseed extension activity seed production:

Certified Seeds: 110 Quintal of certified seed of PKVNL – 260 was produced with the help of Gajanan Maharaj Linseed Growers association under Participatory Plant Breeding program by Dr. Ghorpade at Chikhalapar District Nagpur.

Foundation Seeds: 4.5 Quintal of Foundation Seed of PKVNL – 260 was produced through "Gajanan Maharaj Linseed Growers Association, Chikhlapar", Dist. Nagpur. The monitoring was done for genetic purity of seed at different stages of crop growth in January – Feb 2019.

Foundation Seed Plot - PKVNL - 260

PKV-NL-260 Linseed Production:

The seed was processed, bagged and distributed to farmers for sowing in October/November 2018 (Rabi 2018-2019) in various districts of Maharashtra and Karnataka on total 570 Acres for commercial cultivation (Table 9).

Table 9: PKV-NL-260 Linseed Production

Sr. No.	Name of District	Area under Cultivation
1	Nagpur (MS)	280 Acres

2	Chandrapur (MS)	55 Acres
3	Gadchiroli (MS)	60 Acres
4	Bhandara (MS)	35 Acres
5	Wardha (MS)	50 Acres
6	Amravati (MS)	15 Acres
7	Karnataka	75 Acres
	Total	**570 Acres**

Seed Plot - PKVNL – 260

Farmers Training:

Farmer training was organised by Agro-Vision in November 23-26, 2018. ***Dr. Ghorpade*** and Dr. Lambat gave talk on **"जवस -सुधारित लागवड तंत्रज्ञान व मूल्यवर्धन"** ***at 10th Agrovision*** - (November, 2018, Nagpur)**.** Agrovision is organized under the able guidance of Hon'ble Shri Nitin Gadkari, Chief Patron, Agrovision; Minister of Road Transport and Highways; Shipping, GoI and Dr. C.D. Mayee, Chairman - Advisory Council, Agrovision. Agrovision is supported by Ministry of Agriculture, GoI; Ministry of Food Processing Industries, GoI & Govt. of Maharashtra. ***Under linseed session more than 500 farmers attended workshop in Agrovision.***

Evaluation of high oleic safflower variety developed under ICAR-NASF project by CINHD:

CINHD along with NCL, Pune and NARI-Phaltan developed safflower variety (non-genomic approach) which was characterized as high oleic (75% oleic acid content). This variety was grown at Chikhlapar, Nagpur district for genetic purification for oleic content and multiplication of its seed for its eventual commercial utilization

High Oleic Safflower Variety

Krishi Melawa:

Krishi Melawa was organised by **Rotary Club, Nagpur** at Chikhlapar, under the Chairmanship of Former Joint Director of Agriculture, Maharashtra State **Dr. P. N. Raut** for promotion of linseed and its value additions. **Dr. P. B. Ghopade** presented work done by ICAR-AICRP Value Addition Centre, IRSHA, Bharti Vidyapeeth (Deemed to be University), Pune.

Any other activities:

1. Dr. Sadhana Joshi, Professor and Head from Mother and Child Health, BVDU, IRSHA was awarded the 9th Dr. Rajammal P. Devadas Memorial Award and delivered the oration lecture during the National Institute of Nutrition Centenary year and 50th Annual International Conference of Nutrition Society of India. This award was given for her outstanding contributions in the field of applied nutritional sciences as evidenced by peer review publications, projects handled and high academic pursuit.

2. Two students were supported for B. Sc. (Agriculture Biotechnology- Vidya Pratishthan College of Agricultural Biotechnology, Baramati, affiliated to Mahatma Phule Krishi Vidyapeeth, Rahuri) for partial dissertation in CINHD under guidance of Dr. Anand A. Zanwar.
    i. Ms. Pooja Shitole
    ii. Ms. Divyashree Kadam

3. Mr. M. L. Panse was interviewed by global linker and interview published in their house magazine. Interview link is given below:
    a. Making India “healthy wealthy & wise” is the mission of this innovative foundation-31st July 2018
    b. Let food be your medicine: Diet for disease prevention-9th October 2018
    c. Health Benefits of ALVEL Omega 3 Chocolate Date : 25th August 2018
    d. Key to success for small organizations. Date : 19th Dec.2018
        i. https://icicibankbizcircle.globallinker.com/bizforum/article/making-india-healthy-wealthy-and-wise-is-the-mission-of-this-innovative-foundation/18157
4. Workshop attended on “Good Documentation practices” organized by Regulatory Information & Facilitation Center (RAFC), Venture Center, Pune

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

Visitors and relevant photographs:

International Yoga Day celebration: Talk by Dr. Mihir S. Hajarnavis

Inauguration of ICAR- Quinquennial Review Team (QRT) meeting:

Monitoring visit of ICAR- Quinquennial Review Team members:

Participants of ICAR- Quinquennial Review Team (QRT) meeting:

Dignitary visit to lab

Honorable Chancellor Sir and vice-chancellor Sir attended QRT members:

Honorable vice chancellor sir addressing to QRT participants

Collaborations:

International Collaborations: 6

Sr. No	Name of the Collaborator	Period of Collaboration	Objectives	Status
1.	Dr. M-D Filippi Associate Professor Division of Experimental Hematology and Cancer Biology Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA	September 2018 to August 2023	Mentor on Wellcome DBT India alliance fellowship 1. To establish transgenic mouse model to study mitochondrial metabolism in HSCs in obesity. 2. To study mitochondrial inheritance during cell division in HSCs in obesity. 3. To study signaling	Ongoing

			pathways involved in HSCs– mitochondrial metabolism during obesity.	
2	Columbia University, new York, USA, BVDU, Pune	Collaboratively research and development of the following projects: Infection resistant low cost urinary catheter A topical antimicrobial /wound healing cream	20th January 2015 to 2020	Ongoing
3	Columbia University, New York, USA and Blue Neem Medical Devices Pvt. Ltd Co. Bangalore	Technology transfer and commercialization	18th December, 2015 to 2020	Ongoing
4	Columbia University, new York, USA	Protection of US patent application (PCT/US2017/03196, filed on May 10, 2017) jointly Columbia University, new York, USA and BVDU, Pune and seek to license for commercialization	16th January, 2018 till patent rights expire	Ongoing
5	Prof. Caroline Fall		Advisory member on ICMR-CAR project 2017-2021	Ongoing
6	Prof. Clive Osmond		Advisory member on ICMR-CAR project 2017-2021	Ongoing

National Collaborations: 13

Sr. No	**Name of the Collaborator**	**Period**	**Objectives**	**Status**
1	Dr. Girish Tillu, CCIH,	2016 till date	Scientific and technical inputs	Ongoing

	University of Pune		for developing project proposals, Network pharmacology of Ayurvedic formulations	
2	Dr. Yogesh Shouche, NCMR-NCCS, Pune	2016 till date	Microbiome analysis	Ongoing
3	Dr. Satish Polshettiwar, MIT Pharmacy College, Pune	2018 till date	Drug permeability study, Spectroscopic analysis	Ongoing
4	Dr. Vaishali Deshmukh, Pune	2016 till date	Expert opinion for all ongoing projects from endocrinology perspective Diabetes/obesity aAwareness Activities	Ongoing
5	Dr. Nilesh Shah	2016-2019	Expertise in the field of Homeopathy medicine	On going
6	Dr. Gazala Mulla	2018-2021	Expertise in the field of Unani medicine	On going
7	Dr. Swati Shinde	2018-2021	Expertise in the field of Homeopathy medicine	On going
8	Dr. Supriya Bhalerao	2017-2020	Expertise in the field of Ayurvedic medicine	On going
9	Dr. R. Bankar Scientist D National Centre for Cell Science (NCCS), Pune, India	September 2018 to August 2021	1. To establish diet induced obesity mouse model. 2. To study role of mitochondrial metabolism in HSC function.	Ongoing
10	Dr. V.P. Kale Head and Professor, Symbiosis Centre for Stem Cell Research, Symbiosis International University. Ex scientist G, NCCS	September 2018 to August 2023	Mentor on Wellcome DBT India alliance fellowship 1. Adviser and reviewer of Wellcome DBT project	Ongoing
11	Dr. L.S. Limaye Ex scientist G, NCCS	September 2018 to August 2023	1. Adviser and reviewer of Wellcome DBT project 2. To perform flow cytometry based analyses of mitochondrial function in HSCs during obesity.	Ongoing

12	Dr. C.S Yajnik, KEM Hospital and Research Centre, Diabetes Unit, Pune	March 2017-Feb 2021	Advisory member on ICMR-CAR project	Ongoing
13	Dr. Giriraj Chandak, Senior Scientist, CCMB, Hyderabad	March 2017-Feb 2021	Co PI on ICMR-CAR project	Ongoing

MOU's and Linkages: 03

Sr. No	Name of the Partner	Objectives	Status
1	Jeevanrekha Ayurved Chikitsalaya and Research center, Aurangabad.	To initiate joint multidisciplinary research to begin with in areas given below. Cardio-metabolic risk with special focus on Obesity Other projects/studies would be taken up to include areas as mutually agreed upon	Signed in June 2019
2	Tilak Ayurveda Mahavidyalaya	To carry out collaborative Research activities	Signed in June 2019
3	Dr. Rajiv Chikate Department of Chemistry, MES college, Pune.	Sharing of research facilities	Completed

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. Debashis Mitra, Scientist G, NCCS, Pune.	DBT nominee
Dr. Harshad Patil Associate Professor, Department of Communicable Disease, IRSHA.	Member Secretary
Dr. Kunal Lahiri, Head of the Department, Department of Microbiology, Bharati Vidyapeeth Medical College and Hospital, Pune.	Outside Expert
Dr. Supriya Bhalerao Associate Professor, Department of Obesity, IRSHA.	Biosafety Officer
Dr. Vidya Arankelle Senior Scientist, IRSHA, Bharati Vidyapeeth University, Pune.	Internal Experts
Dr. Harshad Patil, Associate Professor, IRSHA, Bharati Vidyapeeth University, Pune.	
Dr. Ruchika Kaul-Ghanekar Associate 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

Environment, Health & Safety (EHS) In Institutional Committees

Name and Designation	Role
Dr. Supriya Bhalerao, Associate Prof. Obesity and Diabetes Department, IRSHA.	Chairperson

Mrs. Vaishali Kadam, Office Superintendent, IRSHA	Secretary
Dr. Divya Tiraki, Assistant Prof., NCIT, IRSHA	Member
Dr. Amrita Khaire, ICMR RA, IRSHA	Member
Eng. Rahul Kadu , Maintenance Engineer, NCIT, IRSHA	Member
Mr. Tushar Bhosale, Data Entry Operator, Dengue Project, IRSHA	Member

Staff information

Staff Category	Number
Scientific staff	19
Technical Staff	19
Ph.D. students	17
Project Staff	09
Administrative	11
Total	48

Scientific Staff:

Sr. No.	Name of the Staff	Designation	Sign
1	Dr. Akhileshchandra Mishra	Director	
2	Dr. Vidya Arankalle	Senior Scientist	
3	Dr. Sadhana Ramchandra Joshi	Professor	
4	Dr. Ruchika Kaul-Ghanekar	Associate Professor	
5	Dr. Suresh Dnyandeo Jagtap	Associate Professor	
6	Dr. Supriya Bhalerao	Associate Professor	
7	Dr. Shubham Shrivastav	Associate Professor	
8	Dr. Harshad Padmanabh Patil	Associate Professor	
9	Dr. Anvita Kale	Assistant Professor	
10	Dr. Ruta Kulkarni	Assistant Professor	
11	Dr. Deepali Sundrani	Assistant Professor	
12	Dr. Rashmi Govind Virkar	Assistant Professor	
13	Dr. M. V. Hegade	Director CINHD	
14	Dr. P.B. Ghorpade	Emeritus Scientist	
15	Dr. Anand Zanwar	Scientist	

16	Dr. Arnab Kumar Ghosh	Scientist	
17	Ms. Asavari Joshi	Scientist	
18	Mr. Aniket Mali	Jr. Scientist	
19	Mr. M. L. Panse	Director of Research Lab.	

B) Name of the Technical Staff:

Sr. No.	Name of the Staff	Designation	Sign
1	Dr. Prerna Raina	Senior Research Assistant	
2	Dr. Poonam Ashish Gupte	Senior Research Assistant	
3	Mrs. Kamini Dhanesh Dangat	Research Assistant	
4	Dr. Abhijit Avinash Ghadge	Research Assistant	
5	Mrs. Hemlata Mahadeo Pisal	Research Assistant	
6	Ms. Anuradha Rajendra Mulik	Research Assistant	
7	Dr. Sarika S. Mane	Research Assistant	
8	Mr. Kartikey Tanaji Jagtap	Research Assistant	
9	Mrs. Karuna N. Randhir	Technical Assistant	
10	Ms. Vrushali Kadam	Technical Assistant	
11	Ms. Shruti Vidhyadhar Koparkar	Technical Assistant	
12	Ms. Kavita B. Shinde	Technical Assistant	
13	Mrs. Shama Aphale	Technical Assistant	
14	Ms. Shital Ashok Giramkar	Technical Assistant	
15	Ms. Surabhi Subhod Dalvi	Technical Assistant	
16	Ms. Rahat Rizwan Ahmad Khan	Technical Assistant	
17	Mr. Yogesh Badhe	Project Assistant	

18	Ms. Sunita Bhise	Project Assistant	
19	Mr. Pramod Farde	Technical Assistant	

C) Name of the Administrative Staff:

Sr. No.	Name of the Staff	Designation	Sign
1	Mrs. Vaishali Sandip Kadam	Office Superintendent	
2	Mr. Vijaychand Pandurang Gavade	Sub Accountant	
3	Mr. Ananda Dinkar Jadhav	Junior Clerk	
4	Mr. Nitin Shankar Mote	Junior Clerk	
5	Mrs. Anjali Rajendra Gajare	Junior Clerk	
6	Mr. Dilip Kaka More	Trainee Clerk	
7	Mr. Shivaji Dhondiram More	Electrician	
8	Mr. Ankush Rambhau Chandere	Driver	
9	Mr. Jagannath Tukaram Yadav	Peon	
10	Mr. Tushar Ashok Shinde	Peon	
11	Mr. Ravindra Balasaheb Mulik	Animal House Attendant	

D) Name of the Project Staff & Fellowship Staff:

Sr. No.	Name of the Staff	Designation	Sign
1	Dr. Amrita Ankush Khaire	Research Assistant-ICMR	
2	Dr. Suhas Tukaram Mhaske	Research Associate-DHR	
3	Dr. Ashwini Laxman Kamble	Women Scientist-WOSA DST	
4	Dr. Ashwini Hinge	Fellow- DBT Wellcome	
5	Mr. Chetan Popat Chavan	Research Technician-DBT Wellcome	
6	Mr. Rahul Rohidas Mahajan	Lab Attendant	
7	Mrs. Neha Rohit Parkhe	Yoga Instructor-DST SATYAM	
8	Ms. Aishwarya Rajan Kharkhanis	Project Assistant-DBT	
9	Ms. Akriti Sahay	SRF-DBT Fellow	

10	Ms.Shruti Jawale	SRF-DST Inspire Fellow	
11	Mrs. Apoorva Parimoo	SRF-AYUSH Fellow	
12	Ms. Anjali Tukaram Jadhav	SRF- ICMR	
13	Dr. Tanuja Balkrushna Sawant	SRF- DST SATYAM	
14	Mrs. Shridevi Gundu	SRF-DBT	
15	Ms. Vaishali Kasture	JRF-DST Inspire Fellow	
16	Ms. Anindita Nandi	JRF-UGC Fellow	
17	Ms. Juhi Nema	JRF-CSIR-UGC Fellow	
18	Ms. Kinjal Dave	JRF-CSIR-UGC Fellow	
19	Mr. Amol Rajendra Choudhari	JRF-DBT	
20	Mrs. Nidhi Sharma	JRF-EMR AYUSH UNANI Fellow	
21	Ms. Rupika Rajesh Pawar	JRF-EMR CCRH AYUSH Fellow	
22	Ms. Amrita Ulhe	JRF-DST SERB Fellow	
23	Ms. Shubhangi Harke	JRF- DST SATYAM	
24	Ms. Sayali Vedpathak	JRF- DBT BIOCARE	
25	Ms. Abhilasha Umakant Dolle	JRF-AYUSH EMR	
26	Ms. Akanksha Mahajan	JRF	

E) Dengue Project Staff:

Sr. No.	Name of the Staff	Designation	Sign
1	Dr. Hemangi H. Divekar-Sutar	Scientist'B'	
2	Mr. Rahul Lalaso Patil	Health Educator	
3	Ms. Prajakta Sanjay Rane	Research Assistant	
4	Ms. Shreoshri Bhattacharjee	Research Assistant	
5	Ms. Shweta Chelluboina	Research Assistant	
6	Mr. Pravin Maharudrappa Kore	Information Assistant	
7	Mr. Tushar Lala Bhosale	Data Entry Operator	
8	Ms. Anuradha Vijay Kokane	Data Entry Operator	
9	Ms. Meghana Jagdish Walke	Data Entry Operator	
10	Ms. Prajakta Rajaram Jagtap	Data Entry Operator	
11	Ms. Karuna Singh	Data Entry Operator	

12	Ms. Rucha Sakpal	Data Entry Operator	
13	Ms. Vaishnavee Bagde	Data Entry Operator	
14	Mrs. Santoshi Sameer Shinde	Upper Division Clerk	

F) Advance Research Project Staff:

Sr. No.	Name of the Staff	Designation	Sign
1	Dr. Asawari Nandkumar Kanade	Consultant	
2	Dr. Nisha Wadhwani	Scientist-B	
3	Ms. Rutuja Tope	Nutritionist	
4	Ms. Sakshi Selukar	Nutritionist	(Promoted) Joining on 01/07/2019
5	Ms. Madhura Sarda	Psychologist	
6	Mr. Sagar Bhosale	Social Worker	
7	Ms. Prachi Joshi	Social Worker	(Promoted) Joining on 01/07/2019
8	Ms. Anupam Poddar	Lab Assistant	
9	Ms. Shweta Madiwale	Research Assistant	(Promoted) Joining on 09/07/2019
10	Ms. Aditi Mane	Lab Assistant	
11	Ms. Aditi Godhamgaonkar	Lab Assistant	Joining on 01/07/2019
12	Mr. Mahesh Balu Funde	Data Entry Operator	
13	Mr. Nganthoi Elangbam	Data Entry Operator	
14	Mr. Aniket Shelar	Field Attendant	

G) NCIT Project Staff:

Sr. No.	Name of the Staff	Designation	Sign
1	Dr. Archana Prasad Munje	Assistant Professor	
2	Dr. Divya Arvind Tiraki	Assistant Professor	
3	Ms. Anamika Solaskar	Technical Assistant	
4	Mr. Aniket Uttamrao Amlekar	Technical Assistant	

5	Mr. Shambhu Raje Pisal	Technical Assistant	
6	Mr. Rahul Harishchandra Kadu	Maintenance Engineer	
7	Ms. Shital Ramkrishna Nikhar	Qualitive Assurance Executive	
8	Mrs. Prajakta Rishikesh Jaswante	Office Assistant	
9	Mrs. Yasmin Shabbir Attar	Multitasking Staff	
10	Mr. Amol Kondibhau Ohol	Multitasking Staff	
11	Mr. Mahesh Vitthal Humbe	Multitasking Staff	

Ph.D. Students

Sr. No.	Name of the Student	Topic	Status	Under the Guidance of	Year of Registration
1	Mr. Prakash Mansara	Regulation of tumor growth through nutritional intervention involving omega-3 fatty acids	Ongoing/ Thesis Submitted	Dr Ruchika Kaul-Ghanekar	2012-13
2	Mrs. Shama Aphale	Pre-clinical safety evaluation, in-vitro and in-vivo antitumor efficacy and immunomodulatory studies of a herbal formulation in cervical cancer.	Ongoing/ Thesis Submitted	Dr Ruchika Kaul-Ghanekar	2012-13
3	Ms. Dhanashri Ingale	Exploring modulation of Matrix metalloproteinase through herbal and Ayurvedic formulation using cultured Synoviocytes	Ongoing	Dr. Suresh Jagtap	2012-13
4	Ms. Megha Salunke	Inflammatory markers and oxidative stress parameters in Obese individuals and effect of	Thesis submitted	Supriya Bhalerao	2012-13

		herbal intervention on these markers			
5	Mr. Suresh Khadke	Effect of Pathadi Kashaya, Trimad and Omega-3 Fatty Acids on Diabetic Dyslipidemia	Ongoing/ Thesis submitted	Dr. Aniket Kuvalekar	2013-14
6	Ms. Shruti Jawale	Exploring The Efficacy Of Omega 3 Fatty Acid Supplementation To A Maternal High Fat Diet Deficient In Vitamin B12 Ameliorating The Risk for Impaired Brain Development In Rat Offspring	Ongoing	Dr. Preeti Chavan	2014-15
7	Ms. Kamini Dangat	Breast milk components and neurodevelopmental risk in offspring born to mothers with preeclampsia	Ongoing	Dr. Preeti Chavan	2014-15
8	Ms. Anindita Nandi	Association of Vitamin D and fatty acid metabolism in Pre-eclampsia	Ongoing	Dr. Sadhana Joshi	2015-16

9	Ms. Vaishali Kasture	Association of inflammatory markers and one carbon metabolism in Pre-eclampsia	Ongoing	Dr. Sadhana Joshi	2015-16
10	Ms. Varsha Shetty	Synthesis, characterization, in vitro and in vivo studies of cinamaldehide tagged iron nano particles conjugated with folate and FITC for targeted delivery in breast cancer	Ongoing	Dr Ruchika Kaul-Ghanekar	2015-16
11	Ms. Minal Mahajan	Role of selected phytochemicals in regulation of aberrant lipid metabolism in prostate cancer	Ongoing	Dr. Ruchika Kaul-Ghanekar	2015-16
12	Ms. Shital Giramkar	Evaluation of the effect of Triphala on Obesity associated Cognitive impairments	Ongoing	Dr. Supriya Bhalerao	2015-16
13	Ms. Mrunal Gosavi	Development of adjuvanted chikungunya vaccine for systemic delivery.	Ongoing/Course work Completed	Dr. Harshad Patil	2017-18
14	Mr. Kartikey	Studies in	Ongoing/Cours	Dr. Suresh	2017-18

	Jagtap	vidanga - Traditionally used plants with respect to their Pharmacology Activities-	e work Completed	Jagtap	
15	Mr. Manoj khavate	Standardization of selected Embelia spp (Vidanga) . Traditionally used Herbal medicine.	Ongoing/Course work Completed	Dr. Suresh Jagtap	2017-18
16	Mrs. Asavari A. Joshi	Developing and Evaluating the Effects of Omega-3 Edible Oil Blends in Cell Culture Models	Ongoing/Course work Completed	Dr. Anand A. Zanwar	2017-18
17	Mr. Amol Chaudhary	Topic yet to be finalized	Ongoing/Course work Completed	Dr. Ruchika Kaul Ghanekar	2017-18
18	Ms. Anjali Jadhav	Association of maternal nutrition with growth factors and cognitive performance in Preeclampsia	Ongoing/Course work Completed	Dr. Sadhana Joshi	2017-18
19	Ms. Juhi Nema	Maternal Vitamin D and its Association with Angiogenesis in Preeclampsia	Ongoing/Course work Completed	Dr. Sadhana Joshi	2017-18
20	Ms. Kinjal	Association of	Ongoing/Cours	Dr. Sadhana	2017-18

	Dave	one carbon metabolites with placental epigenetic patterns in preeclampsia	e work Completed	Joshi	
21	Ms. Amrita Ulhe	Topic yet to be finalized	Ongoing/Course work Completed	Dr. Ruchika Kaul Ghanekar	2017-18
22	Ms. Apoorva Parimoo	Topic yet to be finalized	Ongoing/Course work Completed	Dr. Ruchika Kaul Ghanekar	2017-18
23	Ms. Akansha Mahajan	Topic yet to be finalized		Dr. Ruchika Kaul Ghanekar	2018-19
24	Ms. Prajakta Patil	Topic yet to be finalized		Dr. Ruchika Kaul Ghanekar	2018-19
25	Ms. Rama Rajadnya	Topic yet to be finalized		Dr. Ruchika Kaul Ghanekar	2018-19