

RESEARCH HIGHLIGHTS

1. COMMUNITY STUDIES

1.1 Nutritional status of below five year old children in the state of Meghalaya

The Government of Meghalaya is contemplating to develop State Nutrition Policy and develop a plan of action for implementation of district level strategy, to improve the nutritional status of children. Therefore, a study was carried out in all the 7 districts of the State. Only 37% of the deliveries were institutional and rest of them (63%) took place at home and 11% of the babies born were with low birth weight (<2.5 kg). Half of the newborns were breastfed within an hour of delivery and none of the infants exhibited any nutritional deficiencies. The overall prevalence of underweight, stunting and wasting was 21%, 44% and 5% respectively, which were lower than the national figures.

1.2 Sensory evaluation and acceptability of locally produced ready- to-eat supplementary foods for beneficiaries of ICDS in the age group of 12-35 months: A study in the Ranga Reddy District of Andhra Pradesh

Two new skim milk based ready to eat supplementary food products with different combination of cereal's, pulse's, skim milk, sugar and fat ratios and fortified with micronutrients (Product 1 - 50:05:10:25:10 & Product 2 - 55:05:10:20:10), were developed by AP Foods Ltd., for management of undernutrition among young children. These products were assessed for their sensory properties and acceptability, in comparison to the currently existing soy based ready to eat supplementary food (Modified Therapeutic Food, MTF - 45:20:00:25:10) of the ICDS-WDCD, Government of Andhra Pradesh. The mean sensory scores given by Mother's Panel for all the sensory attributes including overall palatability was significantly ($p < 0.001$) higher for product 1, followed by product 2 as compared to MTF. Based on 3-criteria priori set for product's, product 1 appears to be more acceptable, suggesting its long term adherence over a 14-day period. It is recommended that this product should be supplied weekly in individual sealed package, and service providers need to impart education to caregivers on handling, usage and storage of the same. Accordingly, the Govt. of Andhra Pradesh is supplying the food for more than 20 lakh children daily.

1.3 A rapid assessment of nutritional status of under five year old tribal children and women of Attappady hills, Palakkad district of Kerala and causes of infant deaths by ICMR Verbal Autopsy Guidelines (Rapid Survey)

There were reports in the media about unusual number of infant deaths, occurring among tribal families in the Attappady Block of Palakkad District in Kerala in 2013. A rapid nutrition assessment was conducted, in May 2013, among children and mothers of the above tribe to ascertain the cause of infant deaths. The food and nutrient intake of the tribal population was lower than the recommended levels. The extent of deficit in micronutrients such as iron, vitamin A, riboflavin and free folic acid was higher. The prevalence of underweight, stunting and wasting among <5 year children was higher compared to other tribes as well as their rural counterparts. The study revealed that, high maternal undernutrition (48% had BMI<18.5). During one year preceding the survey, 10 abortions/still births, 11 neonatal deaths and 3 infant deaths were reported. The major cause of stillbirths and abortions was attributed to pregnancy induced hypertension (PIH) and diabetes, followed by premature delivery and accidental death. For neonatal deaths, the major cause revealed was PIH, premature delivery, and ante-partum haemorrhage, obstructed labour and congenital anomaly. Lapses in healthcare delivery system were identified and reported for corrective measures.

2. BIOSTATISTICS AND BIOINFORMATICS

2.1 Meta-analysis approach on micro-nutrients, food fortification and its effect on health, social and economic factors- A statistical model building

A meta-analysis of randomized, controlled iron fortified feeding trials, that evaluated hemoglobin (Hb) concentration using meta-regression analysis, indicated that the duration of the study was positively related to the effect size (Regression coefficient =0.368; (95% CI: 0.005, 0.731), $p < 0.05$). The net pooled effect size marked after removing the confounders was 4.74 g/L (95% CI: 3.081, 6.399). Association was observed between intakes of iron fortified foods on Hb concentration in children less than 10 years of age. Iron fortified foods could be an effective strategy to mitigate iron deficiency anemia in children.

Further, when evidence from parallel and cross-over randomized controlled trials were combined, to assess the impact of iodine fortified foods on urinary iodine concentration (UIC) in children, meta-regression analysis indicated that dose of feeding was positively related to the effect size (regression coefficient=0.014; 95% CI 0.003, 0.026; $p < 0.019$). There was an association between intakes of iodine fortified foods and UIC in children.

3. MICROBIOLOGY AND IMMUNOLOGY

3.1 Effect of fructo-oligosaccharide coated probiotic on fetal immuno-programming and other health benefits

This study explored fetal immune programming with probiotic and prebiotic (Synbiotic) supplementation in pregnant dams. The results indicated that, in the F0 generation there was a significant ($p < 0.05$) improvement in the T cell proliferation with synbiotic (*Lactobacillus rhamnosus* GG and Fructo-oligosaccharide) supplementation compared to the control group. Interestingly, this improvement in the cell mediated immunity (T cell proliferation response) ($p < 0.05$) continued even in the F1 (pups bred from F0 that received synbiotic) generation though the F1 pups did not receive synbiotic supplementation.

However, immune response against specific antigen (Hep-B surface antigen) showed significant ($p < 0.05$) improvement only in those F1 (pups from F0 that received synbiotic) group that was given synbiotic supplementation though this improvement failed to appear in the group that was not supplemented with synbiotic though, their mothers received the supplementation during pregnancy. No significant improvement in cell mediated immune response was observed when compared to the control group both in treated and untreated probiotic groups of F1 generation. In the F1 generation (pups from F0 that received probiotics) which were given probiotic supplementation there was increased ($p < 0.05$) immune response against specific antigen (Hep-B surface antigen) but only next to Synbiotic group; and this effect was observed even in the F1 (pups bred from F0 that received probiotics) generation that did not receive probiotic supplementation.

Cell mediated immunity showed intergenerational effect with synbiotic supplementation and this improvement in pups (F1 generation) was associated with Bifidobacterial colonization. In contrast, the antibody response to Hep-B surface antigen showed intergenerational effect in pups (F1 generation) born to probiotic supplementation suggesting fetal immune programming with probiotic supplementation.

3.2 Development of tools to identify and map IgE binding epitopes using synthetic peptides.

As part of the study, sequencing and transcriptome analysis of brinjal or eggplant (*Solanum melongena L*) fruit was done to identify allergenic genes and proteins. From the total RNA, unwanted RNAs (rRNA, tRNA and other small RNAs) were removed and qualified Brinjal fruit mRNAs (qualified by Qubit Analyzer) were used, to pair end library preparation and were sequenced on Illumina HiSeq 2500. There were a total of 89,763,638 raw reads in brinjal fruit. Of them, 149224 (Level 3 assembly) were found to be clean reads after filtering. On analyzing the assembly length distribution of brinjal fruit transcripts, most of the sequences were observed between 100-500 and, few sequences were 3000-4000 nucleotides length and the highest sequence length was 10795 (1 sequence). Of the

Immune response in F1 generation

F0	<i>Lactobacillus rhamnosus</i> GG and Fructo-oligosaccharide (Synbiotic) supplementation in F0		<i>Lactobacillus rhamnosus</i> GG (probiotics) supplementation in F0	
F1 pups	Synbiotic supplemented	Synbiotic not supplemented	Probiotics supplemented	Probiotics not supplemented
CMI (T cell proliferation) in F1 pups	Increased	Increased	Comparable to control	Comparable to control
Antibody response to Hep-B surface antigen in F1 pups	Increased	Comparable to control	Increased	Increased

149224 sequences identified from brinjal fruit by transcriptome analysis, 6804 sequences were annotated and were found to be functional genes. Of the 6804 sequences, the exact functions were identified for 1053 sequences by mapping. From the total sequences, 72625 sequences had Basic Local Alignment Search Tool (BLAST) hits and were matching with existing databases. However, 68742 sequences were newly identified and did not have any Blast hits with existing databases.

3.3 Regulatory T cell (Cd4/ Cd25/ CD127-/ FOXP3) population and B cells with Cd23/ CD21 expression in pregnant women with vitamin D deficiency and their newborns

The study hypothesised that low levels of vitamin D would be associated with impaired regulatory T cell function and increased an amount of B cells with CD23/CD21 expression, resulting in higher risk of asthma/allergy. It explored Treg cell function, CD23/CD21 expression and VDR expression in pregnant women with vitamin D deficiency. The results indicated that of the total T cell population, the proportion of the regulatory T cell population (CD4/CD25/CD127-/FOXP3) was significantly ($p < 0.05$) lower in vitamin D deficient subjects compared to sufficient and insufficient subjects. Of the total B cells (CD19) population, the proportion of B cell with CD23 expression levels was significantly higher in vitamin D deficient subjects compared to vitamin D sufficient and insufficient. B cells with CD21 expression levels were also significantly higher in vitamin D deficient subjects compared to vitamin D sufficient and insufficient subjects. VDR and FOXP3 gene expressions were down regulated and CD23 and CD21 genes were up regulated in the placenta of vitamin D deficient pregnant women. These results show impaired regulatory T cell function and increased IgE receptors expression, in cord and maternal blood and placenta of vitamin D deficient pregnant women.

3.4 Effect of probiotic supplementation on weight reduction and its impact on micronutrient and immune status in obese subjects

The indigenously prepared probiotic curd in combination with *Lactobacillus bulgaricus* and *Streptococcus thermophilus* showed significant changes in the lipid profile parameters, upon supplementation to obese subjects. There was also an immunomodulation effect in the obese subjects, upon supplementation with probiotic curd.

4. BASIC STUDIES

4.1 Simultaneous determination of biochemical indicators of micronutrient status from the finger puncture blood sample by kits

Dried blood spot collection kit for vitamin A analysis by HPLC and ELISA based serum ferritin estimation kit: Two kits (i) Dried Blood Spot (DBS) for diagnosing Vitamin-A deficiency and (ii) ELISA for ferritin as Marker for assessing bioavailability of iron using Caco-2 cell line (Patent application no. 1927/DEL/2013) were developed. These kits were launched by the Union Health Minister on 20th Feb 2014.

4.2 Characterization of risk factors of anemia among infants and preschoolers from rural India

Project Grow-Smart, a randomized controlled interventional trial, was carried out among infants and pre-schoolers in 26 villages of four state administrative blocks (mandals) from Nalgonda District of Andhra Pradesh (now in Telangana), India. The baseline data was analyzed for estimating anaemia prevalence and severity and to characterize maternal and child factors associated with anaemia in infants (N= 518) and preschoolers (N=326), in preparation for designing an effective anaemia control program. There was high prevalence of anaemia in infants (66.4 %) and preschoolers (47.8%). Determinants of anaemia in infants were male gender, maternal anaemia, low infant ferritin and high c-reactive protein. Maternal anaemia, maternal low education, child age, high c-reactive protein and soluble transferrin receptor were significant risk factors for anaemia in preschoolers. Family-based strategies need to be identified and enforced to tackle this nutritional problem among children.

4.3 Dietary diversification of Indian vegetarian diet to improve iron bioavailability- Studies using Caco-2 Cell line model

The focus of the study was to screen combinations of food groups to formulate a diversified diet high in bio available iron. To further, improve bioavailability of diversified diet Indian herbs were screened using Caco 2 cell line. Identified herbs had iron content ranging from around 10-60 mg/100 g. Among the herbs *B. diffusa*, *L. sativum* and *T. ammi* contained iron above 40 mg/100g but also high amount of tannin/ phytate. *A. racemosus* and *B. diffusa* were selected on account of high iron, contrasting inhibitor contents for testing iron absorption promoting activity. There was no difference in ferritin induction either in the presence or absence of FeCl₃. However, mineral solutions of both the herbs with exogenous an incorporation of ascorbic acid, induced a 10 fold higher ferritin concentration, signifying that these herbs though rich in iron could not effect endogenous and exogenous iron bioavailability. A combination of wheat and rice at a ratio of 1: 3 had the highest iron dialyzability. Among pulses, green gram and lentil had higher percent dialyzability compared to bengal gram or red gram. Addition of these pulses to Bengal gram and red gram enhanced percent dialyzability significantly. These results suggest that the habitual Indian diets can be effectively diversified to enhance iron bioavailability.

4.4 Foetal programming for neuro-musculoskeletal development in the rat offspring: Role of antenatal and perinatal magnesium deficiency

The role of antenatal and perinatal magnesium deficiency in foetal programming, for neuro-musculoskeletal development in the rat offspring was evaluated. It was observed that in the embryos/ offspring of the Mg restricted WNIN rat dams, the brain development was impaired albeit transiently (but not at birth). This appears to negate any role of impaired brain / neuronal development in the changes observed in their body composition in later life. The differential gene expression of Leptin, adiponectin and 11 β HSD1 and the corresponding change in DNA methylation in the embryos, at later time points appear to suggest that maternal Mg restriction induced changes in the body composition of the offspring may be programmed right during the intra uterine growth. The findings suggest that maternal Mg restriction induced alteration of promoter DNA methylation could be a mechanism underlying changes in the expression of relevant genes responsible for adiposity and associated stress.

4.5 Role of the Ubiquitin-Proteasome pathway in vitamin D deficiency induced muscle atrophy and hypoinsulinemia

Vitamin D deficiency leads to muscle wasting in both animals and humans. A vitamin D deficient rat model was created using Sprague Dawley male rats. The involvement of the ubiquitin proteasome and other proteolytic pathways in vitamin D deficiency induced muscle atrophy were studied. To delineate the effect of hypocalcemia, which accompanies D-deficiency a group of deficient rats were supplemented with high calcium alone. Total protein degradation in muscle was assessed by release of tyrosine; proteasomal, lysosomal and calpain enzyme activities were studied using specific substrates by fluorometry, and E2 enzyme expression was assessed by western blot analysis.

Muscle histology was done by myosin ATPase staining method, while 3-methylhistidine in the urine was estimated using HPLC. Muscle gene expression was measured by semi-quantitative RT-PCR. Total protein degradation in muscle and the level of 3-methylhistidine in urine were increased in the deficient group, compared to control group. Proteasomal enzyme activities, expression of the E2 ubiquitin conjugating enzyme and ubiquitin conjugates were increased in the deficient group, compared to controls. On the other hand, lysosomal and calpain activities were not altered. Type II fibre area; a marker for muscle atrophy was decreased in the deficient muscle compared to control muscle. Muscle atrophy marker genes and proteasomal subunit genes were up regulated, while myogenic genes were down regulated in D-deficient muscle. From the results it appears that the ubiquitin proteasome pathway is the major pathway involved in vitamin D deficiency induced muscle protein degradation and that calcium supplementation alone in the absence of vitamin D corrects the changes.

4.6 Isolation and characterization of procyanidine-B2 as a novel antiglycating agent from cinnamon

Previously, it was established that cinnamon has significant potential to inhibit advanced glycation endproducts (AGE) formation, under in vitro conditions. Based on bioassay-guided fractionation, we have isolated and characterized procyanidin-B2 as the active component of cinnamon that is involved in AGE inhibition. The data indicate that procyanidin-B2 enriched fraction, scavenges dicarbonyls. Further, procyanidin-B2 fraction of cinnamon inhibited the formation of glycosylated hemoglobin in human blood under ex vivo conditions.

4.7 Amelioration of diabetic nephropathy in rats, by procyanidin-B2 from cinnamon through inhibition of AGE formation

In this study, the potential of procyanidin-B2 (PCB2) isolated from cinnamon to prevent in vivo accumulation of AGE and to ameliorate renal changes in diabetic rats have been described. Feeding with PCB2 prevented glycation mediated RBC-IgG cross-links and HbA1c accumulation in diabetic rats. PCB2 also inhibited the accumulation of N-carboxy methyl lysine (CML), a prominent AGE in diabetic kidney. Interestingly, PCB2 prevented the AGE mediated loss of expression of glomerular podocyte proteins-nephrin and podocin. Inhibition of AGE by PCB2 ameliorated diabetes mediated renal malfunction in rats, as evidenced by reduced urinary albumin and creatinine.

4.8 Effect of soluble lutein and soluble curcumin against diabetic cataract

Lutein and zeaxanthin are present in macula and lens of the human eye to protect them from oxidative damage and reduce the risk of age related macular degenerations and cataracts. Previously, it was shown that lutein (1%) and curcumin (0.01%) in the diet delayed but did not prevent cataract in diabetic rats. Bioavailability is a major issue for the success of clinical utilization of compounds such as lutein and curcumin. Now, it has been demonstrated that soluble lutein and soluble curcumin are more effective in delaying diabetic cataract compared to their respective regular formulations at the same dose. Increased bioavailability of soluble formulations might explain the observed biological effects.

4.9 Evaluation of WNIN/GR-Ob rat as a model for obesity associated type2 diabetic complications

A series of animal experiments were conducted, with various rodent models to evaluate a suitable animal model to understand the molecular basis of obesity associated diabetic complications. Based on these studies, we report that neonatal-streptozotocin (nSTZ) WNIN-GR/Ob model could serve as a suitable model for studies on obesity associated diabetic complications, and also for conducting dietary intervention studies.

4.10 Development of rapid assays for the detection of genetically modified foods

Genetically modified (GM) crops are gaining popularity across the globe because of their improved agronomic properties and rapidly gaining entry into the food chain of human's and livestock. Consumption of genetically modified food and feed is highly debated as their safety, on long term use

is yet to be established. There is a need to verify presence of biomarkers in GM foods to comply with food regulatory authorities, labeling requirements, safeguard consumers, check unapproved varieties and environmental contaminant. In a Public-Private partnership model with Agilent Technologies, India, PCR-based multiplex and singleplex assays were developed to detect a number of commercially available genetically modified crops in India and abroad. Singleplex PCR assays were developed for the inserted transgenes like NOS, CaMV35S, FMV, cry1AC, Cry1AB, EPSPS and events of cotton (MON531, MON15985), Maize (GA21, Bt-176), Rice (LLrice62), Canola (GT73) and potato (EH 92-527-1). Single tube multiplex PCR assays were developed for cotton and maize. In addition, multiplex PCR assays were also developed to detect multiple GM crops in a single assay when presented as simple admixture e.g. canola and cotton, maize and cotton, rice and canola, rice and potato, canola and maize as well as complex admixture of cotton, potato, canola, rice and maize.

4.11 Assessment of body composition in Indian females using different techniques

The study was designed to validate the existing methods (Hydro-densitometry, Air Displacement Plethysmogram (ADP), Bio-electrical Impedance Analysis (BIA) and Skinfolts (SKF)) to assess body composition and to develop regression equations using skin fold measurement for accurate appraisal of body composition to suite Indian female population. The result of the study revealed that in Preadolescents, there is a good agreement between ADP and BIA when compared to ADP and SKF method. Based on the results, regression equations for fifteen different combinations of skinfold thickness were drawn, suitable to Indian female population.

4.12 Ergonomic study to test the efficacy/suitability of Bicycle Driven Charkha among women spinners

An Ergonomic study to test the efficacy/suitability of bicycle driven charkha among women spinners was a translational study that was carried out, at the request of Khadi and Village Industries Commission, GOI, wherein; the efficacy and suitability of newly developed bicycle driven charkha was tested as against traditional Hand Charkha based on the physiological efficiency, physical work performance and productivity. All the physiological parameters tested to assess the work efficiency of the two modules indicated that though the oxygen consumed (VO_2/min) and over all energy expended (MET) is more in Cycle Charkha, the energy utilised to produce one gram yarn yield is less in cycle charkha (1.552 kcal) compared to hand charkha (2.698 kcal). It was observed that in Cycle Charkha, the women spinners were spending 1.552 kcal for producing one gram of thread as against 2.698 kcal in Hand Charkha for the same amount of produce. Further, it was observed that in Hand Charkha, the spinners could spin 2.25 hanks per hour, whereas, in Cycle Charkha it was increased to 4.99 hanks per hour resulting in 121% increase in their produce. The Cycle Charkha was found to be more efficient, convenient and ergonomically viable over the traditional hand driven charkha.

4.13 Anti-inflammatory potential of dietary n-3 polyunsaturated fatty acids in experimental ulcerative colitis: Biochemical and molecular mechanisms

The study investigated the impact of substitution of n-6 PUFA with n-3 PUFA (α -linolenic acid/EPA&DHA) on inflammatory response in dextran sulphate sodium induced colitis (DSS) in rats. The results showed that substitution of n-6 PUFA with α -linolenic acid (n-6:n-3 ratio of 2) or DHA&EPA (n-6:n-3 ratio of 10), mitigates the DSS induced colitis as evidenced by reduction in neutrophil infiltration, preservation of colonic architecture and reversal of the shortening of the colon length as well as improvements in the clinical symptoms of the colitis. The results of the study reinforce the current recommendations of increasing n-3 PUFA in the diet for the prevention of diet related chronic diseases including inflammatory bowel disease (IBD).

5. PUBLICATION, EXTENSION AND TRAINING DIVISION

5.1 Nutrition education for adolescents: An interventional approach to create awareness on “Eat right and play with might”

The study was conducted to impart education on nutrition and physical activity through participatory approach and peer education using Oorja clubs (school nutrition clubs). After intervention, through

“Oorja club concept” a significant improvement in knowledge related to nutrition and importance of physical activity, was observed among the adolescent trainers. These trainers carried out peer education on nutrition, health and physical activity to their peers in schools. The results indicated a significant improvement in the knowledge on breakfast, importance of nutrition and physical activity. The study demonstrated that integrated nutrition education approach that combines interactive lectures and participatory approaches engaging students peer education can be effective in educating students in nutrition while underscoring the importance of physical activity.

5.2 Nutritional awareness among primary school children: Role of interventional approaches

A study assessed nutritional awareness among primary school children using pictorial questionnaires and evaluated the use of interventional approaches with reiterative colorful imagery and demonstration of live samples of foods. The study showed that the intervention improved not only the children's ability to recognize various foods but also to differentiate between healthy and unhealthy options.

6. FOOD AND DRUG TOXICOLOGY RESEARCH CENTRE

6.1 Prevalence and severity of fluorosis in Doda district, Jammu and Kashmir

Fluorosis, which is a public health problem is endemic in 204 Districts of 21 States of India including the Doda District of Jammu and Kashmir. Scanty information is available on prevalence of fluorosis in Doda District. The fluoride levels were highest in the Golibagh followed by Malwas village resulting in high human intake of fluoride. Dental fluorosis was more common in girls than boys. High level of urinary fluoride excretion was observed in affected individuals. There was also kidney related (Creatinine, Urea) and bone related CALP, osteocalcin, PTH, 25OH vitamin D and 1,25(OH) vitamin D and liver related (AST and ALP) abnormalities in children exposed to fluoride.

6.2 Assessing the thermal stability of oxytocin in milk and digestive stability of oxytocin *in vitro* and *in vivo*

When the thermal stability of oxytocin in milk and digestive stability of oxytocin *in vitro* and *in vivo* was assessed, it was found that there was no thermal degradation of oxytocin due to boiling. *In silico* digestion analysis revealed that pepsin, chymotrypsin and intestinal proteases possess specific proteolytic cleavage sites in oxytocin amino acid sequence while trypsin has no such sites. Pancreatin could significantly digest oxytocin due to serine proteases. The studies also revealed that exogenous OT injections do not influence its content in milk and OT administered orally is rapidly digested in the intestine.

6.3 Fish egg protein hydrolysates as nutraceutical/ health food in promotion of immunomodulatory activities

In the current investigation fish egg waste has been identified as potential source of protein which can become a value added product. The bioactive Protein hydrolysates has been successfully prepared from underutilized rohu fish by using pepsin trypsin and Alcalase enzymes. The compositional analysis of protein hydrolysates revealed that it has good amino acid profile along with essential micronutrients along with presence of ω -3 fatty acids, especially docosahexanoic acid (DHA). The Molecular mass distribution of the hydrolysates showed, presence of low mass peptides below 10 kDa.

The hydrolysates dose dependent antioxidant activity in various *in vitro* models such as 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity, 2,2'-azino-bis(3-ethylbenzthiazoline-6)-sulfonic acid (ABTS+) radical cation scavenging activity, ferric reducing antioxidant power (FRAP), and ferrous ion (Fe²⁺) chelating ability has been observed. The humoral and cell mediated immune responses in BALB/c mice after 45 days of oral administration was recorded. Rohu egg protein hydrolysates suggest an immune-modulatory effect. The study outcome demonstrate's that the fish egg protein hydrolysates has bioactive peptides, with potential health benefits and can become a value added product.

6.4 Evaluation of the impact of genetic polymorphism on pharmacodynamic activity of commonly prescribed antihypertensive drugs (Thiazide diuretics, ACE inhibitors, CCBs and β -blockers)

The study aims to observe the current trends in prescribing patterns of antihypertensive drugs along with its pharmacodynamic activity and in understanding the role of genetic polymorphism. The first part of the study was to monitor the prescription and consumption profile of antihypertensive drugs in Tertiary care hospital. The results of the study demonstrated use of antihypertensive drugs such as monotherapy (57%), ditherapy (35.0%), and multitherapy (8.1%) in patients. The prescription profile indicated preferential order as BBs (atenolol), CCBs (amlodipine), ARBs (telmisartan) and ACEIs (ramipril) in monotherapy. Among the ditherapy, CCBs were most preferred choice of drug which were administered in combination with BBs, ACEIs and ARBs.

The second phase of the study is undertaken by recording all the prescription information and assessing the role of Single Nucleotide Polymorphism in the uncontrolled Blood pressure.

7. NATIONAL CENTRE FOR LABORATORY ANIMAL SCIENCES

7.1 Studies on anti-obesity properties of *Garcinia* species:

Studies on anti-obesity properties of *Garcinia* species indicated that the maximum activity against hyperlipidemia was exhibited at high dose level of *Garcinia indica* (5%). It reduced body fat significantly, without any toxicity. Since this compound is anti-glycating, it helps in correcting insulin resistance. The results of the present study indicate that further studies can be conducted to explore its mechanism of action so that a good anti-hyperlipidemic and anti-glycating agent could be developed.

7.2 Dose and time dependent effects of *Mucuna pruriens*, *linn ethanolic* seed extract on stress related parameters in WNIN/GR-Ob rats

Dose and time dependent effects of *Mucuna pruriens*, *linn ethanolic* seed extract on stress related parameters in WNIN/GR-Ob rats was studied. Physical parameters like growth, food intake, feed efficiency ratio, activity was monitored for the experimental period of 45 days. Physiological parameters like body composition and bone mineral contents were measured. Biochemical parameters like cholesterol, triglycerides and stress markers like serum cortisol and *L-dopamine* were analyzed. Cortisol has many functions. It helps the body use sugar (glucose) and fat for energy (metabolism), and it helps the body to manage stress. By supplementing *Mucuna pruriens* which contains dopamine and improving environmental conditions the animals exhibited less stress levels.

7.3 Evaluation of promising plant extracts and active constituents for anti-obese, anti-diabetic and hepato-protective properties in WNIN/GR-Ob rats

The study evaluated promising plant extracts and active constituents for anti-obese, anti-diabetic and hepato-protective properties in WNIN/GR-Ob rats. There was a significant reduction in the body weights and food intake of animals treated with the plant extracts. Body composition estimation by TOBEC revealed that, there was a significant increase in the lean body mass and reduction in the total body fat content in treated animals compared to controls. However, no significant changes were noted in bone mineral content and density. Hypoglycemia was prominent in *A.indica* extract treated animals, compared to the other experimental animals. Lipid contents like cholesterol and triglycerides decreased significantly in all the treated animals. There was no toxicity observed in the liver of animals treated with the plant extracts. Varying degrees of degeneration of kidney tubules were observed in all the experimental animals as compared to controls and animals treated with *A. indica*.

7.4 Effect of bio-active compounds isolated from *piper nigrum* on high fat diet induced obesity in SD rats – A MRI study

Rats fed with high fat diet when treated with *Piper nigrum* have shown reduced physical parameters like food intake, growth. Significant increase was found in body composition parameters like lean body mass. Decrease in total body fat and % fat was observed in the HFD rats after being treated with

piperine extracts. DXA analysis revealed that there is a significant increase in bone mineral content and bone mineral density. Regional wise fat distribution analysis revealed that there is predominant deposition of fat at retroperitoneal region. The MRI analysis revealed that, there is a significant reduction in the adipose tissue volumes in the whole body and regional adipose tissue volumes i.e., subcutaneous, thoracic, and retro peritoneal. This study of effect of *Piper nigrum* on obesity can be explored further with respect to its mechanism of action to translation research.

8. PRECLINICAL TOXICOLOGY

8.1 Acute toxicity study in mice and sub-chronic toxicity study in rats, *in-vitro* allergenicity test of seed & leaf of transgenic mustard containing Hybrid Dmh-11

Transgenic *brassica juncea* containing barnase, barstar and bar genes has been developed by Centre for Genetic Manipulation of Crop Plants (CGMCP), University of Delhi South Campus (UDSC). As per the Guidelines for safety assessment of genetically engineered plants, 2008, prescribed by ICMR and the accompanying protocols by DBT, the edible plant parts which have the expression of the inserted genes, need to be tested for their safety profile. We have completed the investigations i. Assess potential allergenic Cross-Reactivity by The databases PubMed, Allergen Online version 12.0 Allergen Database and NCBI Entrez Protein Database were used to accomplish the bioinformatics searches. ii. Pepsin digestibility and thermal stability assay of recombinant Bar, Barnase and Barstar proteins, iii. Acute oral toxicity of Recombinant Bar, Barnase and Barstar protein in Swiss Albino Mice. The results of the study indicated a lack of any significant sequence similarity of Barnase, Barstar or Bar proteins to any allergenic proteins. The pepsin digestibility assay showed that all the three recombinant proteins were rapidly degraded by pepsin in SGF, and 90% digestibility was achieved within 0.5 mins. The Bar (1000mg/kg), Barnase (1000mg/kg) Barstar (1700mg/kg) proteins administered once orally at the above concentration to mice, did not show any adverse effect on any of the parameters studied. The subchronic investigations and compositional analysis are in progress to determine the safety of transgenic mustard containing Hybrid Dmh-11.

8.2 Pre-clinical bioavailability and safety evaluation of temozolamide co-crystal

The role of Temozolomide in treatment of malignancies such as melanoma, sarcoma and astrocytomas at clinical level is well established. However, the limitation of usage is due to its very short stability. TMZ Crystalin Research Private Limited has developed, TMZ Co-crystal using Co-crystallization method. Since, this processing modifies physicochemical characteristics of active pharmaceutical ingredients, comparative bioavailability and safety profile is necessary as per the guidelines of Schedule Y of DCGI. The Pharmacokinetic and Toxicokinetic studies was conducted in Sprague Dawley Rats using cross over design. The Acute and Sub-chronic Toxicity test (28 days) has been conducted in healthy Sprague Dawley Rats. The test and reference standard drugs are found to be bio-equivalent with no significant change in C_{max}, AUC and T_{max} between test drug and reference standard drug. The toxicokinetic parameter suggest that, no adverse events based on liver, renal and hematology investigation. The NOAEL in rats has been recorded at 70mg/kg which is 2 times higher than the intended clinical dose. The project is completed and dossiers has been submitted for regulatory approvals to undertake clinical trials.