CHAPTER 6

BIOMEDICINE

Doctoral Theses

030. BIHAQI (Syed Waseem)
Protective Effects of the Extracts of Convolvulus Pluricaulis in a Rat Model of Alzheimer's Disease.
Supervisor : Dr. Manisha Tiwari
Th 16242

Abstract

Investigates the neuroprotective action of aqueous extract of Convolvulus pluricaulis. Showed that aqueous extract of Convolvulus pluricaulis proved to be an efficacious drug in inhibiting the elevated activity of AchE. The extract also corrected the altered the levels of antioxidants. Tau hyperphosphorylation and Cdk5 hyperactivation was also reduced by administration of extract. Altered mRNA levels of protein responsible for normal functioning of neurons were also corrected. Histopathological and immunohistochemical perturbations observed in both models were also corrected. Thus aqueous extract of Convolvulus pluricaulis can be potentially used as a drug to counter act symptoms of AD.

Contents

031. DHIMAN (Neerupma)
Synthesis and Pharmacokinetic Studies of Noscapine Analogs having Antitumor Activity.
Supervisor : Dr. Anju Katyal
Th 16237

Abstract

Synthesizes new analogs of noscapine and study their cytotoxic potential. Also developes an adequately sensitive, specific and selective method for the extraction of noscapine and bromonoscapine from biological tissues for pharmacokinetics and bioavailability analysis. The pharmacokinetic study of noscapine and bromonoscapine point towards nonlinear behaviour of these molecules at high concentrations, which could be due to the saturation of drug transport or metabolic enzyme systems. The bromo analog of noscapine is more bioavailable i.e. almost double as compared to the parent molecule. The improved two fold bioavailable of bromonoscapine over noscapine calls for their clinical advancement as novel anticancer agents.

Contents

032. GUPTA (Pallavi)
PU. 1-Mediated Transcriptional Control of Bone Marrow Derived Human Hematopoietic Stem Cells.
Supervisors : Dr. Daman Saluja, Dr. G. U. Gurudutta and Lt. Gen (Retd.) T. Ravindranath
Th 16236

Abstract

Studies to enhance the differentiation potential of PU.1 by preventing its GATA-1 mediated repression. GATA-1, an erythroid-specific transcription factor, inhibits the transcriptional ability of PU.1 by binding in the β3/β4 region of its DNA binding domain and thereby displacing its coactivator c-Jum, which is crucial for its transactivation potential in myeloid promoters. The GATA-1 mediated repression of PU.1 could be abolished if the critical residues involved in its interaction were identified and mutated with suitable residues. Also studies the effect of overexpression of wild tupe PU.1 and its multants on the differentiation of human bone marrow-derived $CD34^+$ HSCs by assessing the ability of transfected HSCs to express myeloid cell-specific surface marker CD33 after 96 h of doxycycline induction.

Contents

1. Introduction and review of literature. 2. Sequence and structural analysis of PU. 1 protein. 3. Subcloning of wild-type PU.1 into inducible mammalian gene expression vector and generation of PU.1 mutants by site-directed mutagenesis. 4. Regulated overexpression of wild-type PU.1 and its mutants in HSCs and hematopoietic cell lines. Conclusion and Bibliography.

033. JYOTI

Study of Biological Activity of 2, 4-Thiazolidinedione Analogues as Antidiabetic Agents.

Supervisor : Dr. Manisha Tiwari

Th 16241

Abstract

Concludes that of two compounds studied, compound XVIII, which has two methyl groups attached to the phenyl ring, showed remarkable hypoglycemic and hypolipidemic activities. Compound XVIII was also least cyototoxic as revealed by its IC_{50} value. The diabetic rats treated with compound XVIII also showed significant decrease in the activities of anabolic enzymes like G-6Pase and Fruc-1,6 Bpase whereas increase in activities of catabolic enzymes. The effect was even more pronounced than standard drug, rogisilitazone. It was also able to combat the oxidative stress sifnificantly in diabetic animals as compared to compound XX and rosiglitazone. The treatment of diabetic rats with compound XVIII also normalized the basic ultrastructure of pancreas. In all, it can be considered as promising antidiabetic agent with a better efficacy and fewer side effects.

Contents

1. Introduction. 2. Review of literature. 3. Objectives and scope of work. 4. Materials and methods. 5. (a) Evaluation of hypoglycemic and hypolipidemic activities of TZD analogues. (b) Evaluation of cytotoxicity of TZD analogues and effect on lipid profile. 6. Evaluation of effect of TZD analogues on enzyms involved in carbohydrate metabolism. 7. (a) Role to TZD analogues in ameliorating oxidatives stress. (b) Evaluation of TZD analogues induced hepato-renal toxicity. 8. Role of TZD analogues in protection of ultrastructure of pancreas. 9. Summary.

034. KURUPATI (Raj Kumar)
Analysis of the Host Cellular Responses Induced by a Bacterial Toxin.
Supervisors : Dr. Pratibha Mehta Luthra and Dr. Yogendra Singh
Th 16233

Abstract

Explores the role of various stress responses induced by anthrax toxin, leading to cell death, Phosphoproteome analysis was done to identify important signaling proteins involved in regulation of anthrax toxin mediated cell death. To assess the role of mitochondrial dysfunction in anthrax disease pathogenesis mitochondrial proteome was analyzed. Studies bacterial toxin induced stress responses in murine macrophage cell line J774A.1; Phosphoproteome analysis of murine macrophage cells treated with anthrax toxin; Mitochondrial proteome analysis of murine macrophage cell line towards anthrax toxin.

Contents

035. MAHAJAN (Anubha)
Biochemical and Genetic Studies Exploring the Functions of Human Pentraxins and Clotting Factors.
Supervisor : Dr. Pradeep Nahar
Th 16235

Abstract

Focuses to address the biochemical and genetic role of these proteins in human genetic diseases. Identifies molecular events in clotting factor-factor IX and established genotype-phenotype correlation in North Indian hemophilia B families. Defines the allelic spectrum of Factor IX gene in Asian Indians. Explores the role of plasma hsCRP levels as a marker of inflammation in Type 2 Diabetes Mellitus and diabetic hypertension in North Indian population. Tests for genetic association of Single Nucleotide Polymorphisms in clotting factors, pentraxins, and related genes as functional and positional candidates of Type 2 Diabetes Mellitus in North Indian population; for genetic association of

SNPs in clotting factors, pentraxins and related genes with plasma hsCRP levels in North Indian population.

Contents

1. Review of literature. 2. Characterization of molecular events in human clotting factor IX in hemophilia B among North Indian families and establishing genotype-phenotype correlations. 3. Determination of allelic heterogeneity of molecular events in human coagulation factor IX in Asian Indians. 4. Role of plasma hsCRP levels as a marker of inflammation in diabetic Urban dwellers of North India. 5. Association of pentraxins, clotting factors and pentraxin-related genes with type 2 diabetes mellitus in North Indians. 6. Genetic basis of plasma hsCRP levels in North Indian population. Bibliography.

036. MASHOOK ALI

Gene Expression Profiling of ETO Expressing Cells and its Interaction With Chromatin Remodelling Protein Human Sin3B.

Supervisor : Prof. Daman Saluja

Th 16557

Abstract

Concludes that hSin3B is ubiquitously expressed in all cell types and issues. There are atleast two alternate splices forms, one of which was observed only in transformed cell lines. Both the normal as well as spiced forms are differentially expressed in different adult tissues and in nonmalignant and oral cancer tissues. This suggests that Sin3B spliced form may play a role in cancer development and progression. Further shows that N-terminal domains of Sin3B protein interacts with MTG8. Microaaray data shows that overexpression of both MTG8 and MTGR1 differentially regulates genes involved in Axon guidence pathways. This was also confirmed by studying the expression of gene guidence by real-time PCR using transfected cell lines and adult mouse brain tissues.

Contents

1. Expression of human Sin3B. 2. Protein-protein and microarray gene expression profiling of MTG8 and MTGR1.3. Axon guidence pathway. Bibliography.

037. MD. PARWEZ ALAM

Analysis of Transgenic Mice to Study Dynamic Mutation of CGG Triplet Repeats.

Supervisor : Prof. Vani Brahmachari

Th 16239

Abstract

Focusses on delineating the epigenetic events associated with CGG instability. The epigenetic marking addressed included post-replication modification of DNA by methylation at cytosine residues at the CpG dinucleotides and the ability to form basic genetic unit of eukaryotic cells, namely the nucleosomes. The former objective has the bearing on strong association of repeat expansion, DNA methylation and the disease manifestation and the latter, on the most accepted mechanism of CGG repeat expansion, slippage during replication.

Contents

1. Introduction and review of literature. 2. Analysis of CGG transgenics for copy number and integration site for the transgene. 3. Comparative analysis of epigenetic modification of the transgene and mouse endogenous Fmr1. 4. Comparative analysis of nucleosome organization of transgene and mouse Fmr1. 5. Detection of transgene in single oocyte and sperm pool. Bibliography and appendix.

038. PRASHANT SINGH

Novel Routes for the Synthesis of Thiazolidine-2, 4-dione and its Derivatives.

Supervisors : Dr. Anju Katyal and Dr. N. N. Ghosh

Th 16240

Abstract

Synthesizes derivatives of thiazolidine-2,4-dione to improve the solubility and antidiabetic activity. Also optimization of procedure for the synthesis of thiazolidine-2, 4-diones and its derivatives using different types of catalysts and solvents was done. The well known catalysts like boric acid, indium chloride, heteropoly acid are generally used for the synthesis of thiazolidine-2, 4-diones and its derivatives. We found gold and copper nanoparticles are better catalysts instead of conventional used till now for the synthesis of thiazolidine-2, 4-dione and the derivatives. Moreover the yield and time for the reaction were

significantly improved in comparison of the above cataysts. Synthesis of gold and copper nanoparticles can be done by various methods but their synthesis in ionic liquid is best because ionic liquid provide stability to nanoparticles as well time taken by the synthesis of gold and copper nanoparticles is least.

Contents

1. General introduction. 2. Review of literature. 3. Aim and objectives. 4. Synthesis of thiazolidine-2,4-dione and its derivative using gold and copper nanoparticles in ionic liquid and water. 5. Synthesis of charge transfer complexes of thiazolidine-2, 4-dione with sigma as well as pi acceptors and study their thermal as well as electrochemical properties. 6. Energy optimization and QSAR properties of thiazolidine-2, 4-dione and its derivatives. 7. Synthesis and characterization of cross-slinked chitosan and TZD-chitosan nanopolymers using sodium salt of malanodialdehyde as a cross-linker. 8. Summary.

039. SHARMA (Priyanka)
Epigenetic Studies Relating to the Role of Homocysteine in Coronary Artery Disease : Methylation Profiling by CpG Array.
Supervisors : Prof. Vani Brahmachari and Dr. Shantanu Sengupta
Th 16234

Abstract

Evaluates the status of DNA methylation in CAD patients in conjunction with elevated levels plasms homocrysteine and to examine the methylation profile of CpG island in the whole genome using CpG chip analysis, and to assess their potential role in coronary artery disease.

Contents

1. Introduction. 2. Mining literature for a comprehensive pathway analysis : A case study for retrieval of homocysteine related genes for genetic and epigenetic studies. 3. Detection of altered global DNA methylation in coronary artery disease patients. 4. Genome wide DNA methylation profiling for epigenetic analysis in coronary artery disease patients. Bibliography and appendix.

040. VINEET KUMAR

Functional Characterization of MTGR1 : Interaction with Human Sin3B and Regulation of Genes Involved in Cell Differentiation and Growth.

Supervisor : Prof. Daman Saluja

Th 16238

Abstract

Demonstrates that MTGR1 is a co-repressor and interacts with phosphorylated hSin3B through a highly conserved domain called nervy homology domain 2. The MTGR1 downregulates 'Wnt' pathway in a pleotropic manner. It not only up regulates genes responsible for phosphorylation and subsequent degradation of β-catenin but also down regulates β-catenin as well as TCF-4 mediated gene expression.

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