Contents

Abbreviations
List of publications
List of tables
List of figures

S. No.  Page No.
1. INTRODUCTION  1

2. REVIEW OF LITERATURE  7
   2.1 Peptide-based pharmaceutical industry  7
   2.2 Oxidative stress: focus on PD  8
   2.3 Mitochondrial targeted antioxidants/peptides  9
   2.4 Therapeutic approaches for PD treatment  10
   2.5 Neuroprotective gene therapy: achievements and perspectives  12
      2.5.1 Glial cell line-derived neurotrophic factor (GDNF)  12
   2.6 Dopamine receptors  13
      2.6.1 Dopamine D1-like receptor subfamily  13
      2.6.2 Dopamine D2-like receptor subfamily  14
   2.7 Signal transduction mechanisms of dopamine  15
   2.8 Connections of the midbrain dopamine neurons  16
   2.9 Animal Models of Parkinson’s disease  19
      2.9.1 6-OHDA  19
      2.9.2 MPTP and MPP⁺  20
      2.9.3 Paraquat  21
      2.9.4 Rotenone  21
      2.9.5 Transgenetic model  22
   2.10 Neurochemical Assay  22
   2.11 Chemical information of Dopamine HCl  22
   2.12 Mechanism of DCC Coupling  23
2.13 Amino acids analogues as building blocks for peptidomimetics 29
2.14 Dopaminergic Treatments for Parkinson’s disease 30
2.15 L-Dopa Metabolism and Therapy 31
2.16 Clinically Used Dopamine D2 Receptor Agonists 33
2.17 Blood brain barrier 37
2.17.1 BBB transport mechanisms 38

3. EXPERIMENTAL 55
3.1 Materials 55
3.1.1 Chemicals 55
3.1.2 ELISA and enzymatic kits 56
3.1.3 Antibody 56
3.1.4 Equipments 56
3.2 Methods 58
3.3 Chemical Studies 59
3.3.1 Scheme-I 59
3.3.2 Scheme-II 60
3.3.3 Scheme-III 60
3.3.4 Procedures for synthesis of compounds 61
3.4 Pharmacological Studies 69
3.4.1 Animals, group distribution and treatment of Oxotremorine model 70
3.4.2 Animals, group distribution and treatment of 6-OHDA model 73
3.4.3 Surgery 75
3.4.4 Injection of 6-OHDA 75
3.4.5 Postoperative care 75
3.4.6 Symptoms in the 6-OHDA model of Parkinson’s disease 76
3.4.7 Methods used for assessing motor abilities in rats 77
3.4.8 Behavioral studies 78
3.4.8.1 Apomorphine induced rotational behavior study 78
3.4.8.2 Rota Rod study 78
3.4.8.3 Spontaneous locomotor study 78
3.4.9 Neurochemicals study 79
3.4.10 Enzyme Estimations 79
3.4.10.1 Malondialdehyde Estimation (MDA) 79
3.4.10.2 Glutathione Estimation 79
3.4.10.3 Caspase activity assay 80
3.4.11 Dopamine, DOPAC and HVA estimation 80
3.4.12 Immuno-histochemical studies 81
3.4.13 Photography and Image Processing 81
3.4.14 Statistical analysis 82

4. RESULTS AND DISCUSSION 83
4.1 Chemical Studies 83
4.2 Pharmacological Studies 94
4.3 Immuno-histochemical staining 111

5. SUMMARY AND CONCLUSION 118

BIBLIOGRAPHY 122

PUBLICATIONS