CONTENTS

INTRODUCTION 1-5
REVIEW OF LITERATURE 6-62
PERIPHERAL NEUROPATHY
  Classification of Peripheral Neuropathy 6
  Signs and Symptoms of Peripheral Neuropathy 11
  Causes of Peripheral Neuropathy 12
NEUROPATHIC PAIN 12
  Neuropathic Versus Nociceptive Pain 13
  Clinical Symptoms of Neuropathic Pain 14
ALCOHOLIC PERIPHERAL NEUROPATHY 15
  Definition 16
  Prevalence of Alcoholic Neuropathy 16
  Clinical Symptoms Associated with Alcoholic Neuropathy 17
  Potential Complications Associated with Alcoholic Neuropathy 17
  Pathogenesis of Alcoholic Neuropathy 18
     Nutritional Factors Responsible for Alcoholic Neuropathy 19
        Contribution of Metabolic Pathways 19
        Relationship between Alcoholic Neuropathy and Thiamine Deficient Neuropathy 21
        Role of nutritional status other than thiamine deficiency 23
  Direct Toxic Effects of Ethanol or its Metabolites 24
     Role of Acetaldehyde in Alcoholic Neuropathy 24
     Role of Oxidative-Nitrosative Stress 25
     Role of Protein Kinases in Alcoholic Neuropathy 27
     Involvement of MEK/ERK Signaling 29
     Role of Spinal Cord Microglia 29
     Role of Caspases in Alcoholic Neuropathy 30
     Involvement of Glutamate Receptors 31
     Involvement of Opioidergic System 31
     Involvement of HPA Axis 32
     Effects on axonal transport and cytoskeletal properties 33
Therapeutic Strategies for Alcoholic Neuropathy

Vitamin supplementation 34
Symptomatic Therapies 36

ALCOHOL-INDUCED COGNITIVE DEFICITS

Definition and Prevalence 37
Etiopathogenesis of Alcohol-Induced Cognitive Deficits 39
Role of Neuronal Oxidative-Nitroductive Stress 40
Oxidative Stress Mediated Pro-inflammatory Signaling in Brain 41
Activation of NFκB Signaling Pathway 43
Toll Like Receptor-4-induced Neuroinflammation 44
NMDA Receptor Supersensitivity 46
Glia and Alcoholic Neurodegeneration 46
Involvement of Hypothalamic Pituitary axis (HPA) axis 47
Disruption of Growth-Factor Signaling 47
Inhibition of Neurogenesis 48
Disruption in Glucose Transport and Uptake 49
Effects on Cell Adhesion 49
Altered Developmental Regulation of Gene Expression 50
Therapeutic Strategies for Alcohol-induced Cognitive Deficits 51

THERAPEUTIC INTERVENTIONS EMPLOYED IN THE STUDY

Tocotrienol 52
Epigallocatechin Gallate 55
Resveratrol 57
Curcumin 60

AIMS AND PLAN OF WORK 63-64

CHAPTER 1: SUPPRESSION OF OXIDATIVE-NITROSATIVE STRESS MEDIATED NEUROINFLAMMATORY CASCADE IN EXPERIMENTAL MODEL OF ALCOHOLIC NEUROPATHY 65-108

1.1. Introduction 65
1.2. Materials and Methods 68
1.3. Results 80
1.4. Discussion 99