AIMS AND OBJECTIVES

Alcohol-induced oxidative-nitrosative stress mediated inflammatory signalling plays a key role in the development and progression of alcoholic neuropathy as well as associated cognitive deficits both in adults and in neonates with prenatal alcohol exposure (Haorah et al., 2008; Alfonso-Loeches and Guerri, 2011; Persidsky et al., 2011). The cellular, biochemical and molecular mechanisms behind alcohol-induced neuronal damage and cognitive deficit are not fully understood, but several explanations have been proposed including free radical damage (Cohen-Kerem and Koren, 2003; Crews et al., 2004; Haorah et al., 2008a), alcohol-induced neuroinflammation (Alfonso-Loeches et al., 2010; Alikunju et al., 2011), activation of NF-κβ (Crews et al. 2006) and TLR-4 signaling (Alfonso-Loeches et al., 2010), induction of neuronal apoptosis (Jung et al., 2005), NMDA receptor supersensitivity (Prendergast et al., 2004), suppression of growth factors (Breese and Sonntag, 1995), disruption of the hypothalamus–pituitary–thyroid axis (Scott et al., 1998) and inhibition of neurogenesis (Nixon and Crews, 2002). While each pathway may be injurious alone, collectively they cause an imbalance in the mitochondrial redox state of the cell and lead to excessive formation of reactive oxygen species (Jung et al., 2005; Figueroa-Romero et al., 2008). Increased oxidative stress within the cell leads to activation of neuroinflammatory signalling mechanisms which results in translocation of PKC, activation of PKC and NFκβ, DNA fragmentation and ultimately increased neuronal death that are responsible for the behavioral deficits (Izumi et al., 2005; Jung et al., 2005). Thus, a consensus has evolved that oxidative-nitrosative stress and inflammatory cascade are the major culprits involved in the pathogenesis of alcoholic neuropathy and associated cognitive deficits. The incidence and progression of these complications can be halted by using targeted approach against these pathogenic pathways.

The present research work was undertaken to explore four phytochemicals having antioxidant and anti-inflammatory potential for the prevention of alcoholic neuropathy and associated cognitive deficits.
Aims and Objectives

Tocotrienols, an isoform of well established antioxidant, vitamin E and found in rice bran oil and palm oil together with cereal grains, such as barley, oats, and rye; epigallocatechin gallate, a polyphenolic anti-oxidant present in green tea; resveratrol, a natural phytoalexin and a major constituent of grapes, nuts and berries; and curcumin, a principal curcuminoid of the popular Indian spice turmeric, possess potent anti-oxidant and anti-inflammatory activities. The present study is divided into following three chapters.

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

CHAPTER 2: AMELIORATION OF ALCOHOL-INDUCED COGNITIVE DEFICITS BY BLOCKING INFLAMMATORY SIGNALING AND CELL DEATH CASCADE IN BOTH ADULT AND NEONATAL RAT BRAIN

CHAPTER 3: MECHANISTIC INSIGHT IN THE PATHOPHYSIOLOGY AND AMELIORATION IN EXPERIMENTAL MODELS OF ALCOHOLIC NEUROPATHY AND ENCEPHALOPATHY