Introduction

Iron-induced epilepsy model is widely accepted for better understanding of the basic mechanism of human post-traumatic epilepsy (Willmore et al., 1978a,b; 1986; Willmore and Rubin 1981). This model mimics the release of ferric and ferrous ions from extravasated blood after cerebral contusion or head injury. It has been reported that intracortical injection of ferric chloride results in an increase in free radical generation and oxidation of lipids, proteins etc. This disturbs neurotransmitter homeostasis and increase in guanidine compound production. These alterations result in hyperexcitability of neurons which can be diagnosed through electrocorticogram (ECoG) as seizures (high amplitude and high frequency) and behavioral manifestations. In human, traumatic head injury results in induction of spontaneous seizures, months to years after head injury. This latent period has been targeted by neurologists to treat patients with threat to develop seizures. At present, several effective anticonvulsants are available in the market but no promising antiepileptic drug, effective in preventing late seizures is available. A list of antioxidants (Table-2) from plant origin have been proposed to be beneficial in suppressing seizures, but if given as dietary supplements, does have any role in the development and progression of epilepsy is very little known. Therefore, in the present study we have investigated the affect of dietary curcumin and treatment of L-deprenyl in FeCl₃ induced epileptic rats.

Curcumin is a yellow polyphenolic compound extracted from the rhizome of turmeric plant (*Curcuma Longa*). Curcumin is being used since time immemorial as spice in Indian food and herbal medicine in Indian system of medicine “Ayurveda”. Hence it is found that, in India, prevalence of Alzheimer disease (AD) and Parkinson disease (PD) in patients between 70 to 79 years of age is 4.4 fold less than that of the united states (Ganguly et al., 2000). Curcumin’s ability to cross blood brain barrier (BBB) (Yang et al., 2005) and bind to redox metal ions (Baum et al., 2004) lead us to hypothesize that dietary curcumin may have beneficial affect on epilepsy.

In the present experiments, two doses of curcumin, low (500ppm) and high (1500 ppm) were used for long and short term treatment in FeCl₃ induced epileptic rats. Long-term (32 weeks) treatment of curcumin was started three months before FeCl₃ injection while in short-term (5 weeks) curcumin was fed after FeCl₃ injection. In addition to
curcumin, we also assessed the effect of L-deprenyl, a known hydroxyl ion suppressor (Wu et al., 1996) on epileptic rats following same treatment plan.

On the basis of experimentation, present work was categorized into two parts. In the first part, FeCl₃ induced electrophysiological progression of seizures and epileptogenesis related biochemical, behavioral and microscopic alterations were ascertained. In the second part, antiepileptogenic potential of curcumin and L-deprenyl was investigated in the light of 1) Electrophysiology 2) Biochemistry 3) Histology 4) Behavior and 5) correlation parameters as listed in materials and methods.

In electrophysiological studies, progression of seizures in different experimental groups was investigated by employing synchronized video-EEG monitoring. Experimentation was carried out on rats of two age groups, young (4 months) and old (18 months), in order to understand the relationship between aging and epilepsy. Electrophysiological recordings were performed, on both ipsilateral and contralateral side of cerebral cortex and hippocampus (CA1 field) regions of the brain in order to determine the spreading of epileptogenic foci. ECoG records delineate significantly faster spreading of seizures in older rats in comparison to younger ones. We have investigated whether dietary supplement of curcumin does affect development and progression of seizures in young and old epileptic rats. Data derived delivers delayed as well as preventive role of curcumin and L-deprenyl against onset and development and progression of seizures.

In biochemical studies, assays like lipid peroxidation, membrane fluidity and membrane linked proteins (Na-K ATPase activity, Ca²⁺ dependent protein kinase C activity) were measured as they are known to play putative role in development of epileptiform activity. Both curcumin and L-deprenyl were found to inhibit epileptogenic alterations in above mentioned parameters.

In histological studies, light and transmission electron microscopy (TEM) were performed to make out cell counts and visualize ultrastuctural alterations associated with epileptogenesis in different groups of experimental rats. Cellular impairments observed in iron induced epileptic rats were found to be well countered by long-term and short-term treatment of curcumin and L-deprenyl.
In behavioral studies, we investigated epileptogenesis associated memory deficit and increased anxiety behavior by employing Morris water maze (MWM) tests and open field tests. The behavior tests suggested a tight association of memory deficit with electrophysiological and biochemical alterations. Dietary supplement of curcumin and L-deprenyl administration were effective in preventing memory decline and decreasing the anxiety associated with epileptogenesis. In correlation studies, using Pearson correlation matrix we found out relationships between the parameters studied. Correlation tests was performed in all groups viz. FeCl₃ treated, curcumin treated and L-deprenyl treated.

Overall data delineates that vulnerability of cerebral cortex and hippocampus (CA1 field) of the brain for epileptogenesis increases with age. Present study ascertained that the electroencephalogram (EEG) pattern indicating development and progression of epileptic seizures is a collective consequence of biochemical and histological alteration which leads to behavioral alterations in the epileptic rats. Our study indicates that dietary curcumin could be a perspective, safe and more effective for long term treatment and suppression of seizures associated with post-traumatic epileptogenesis than L-deprenyl.