Summary & Conclusions
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The work embodied in this thesis has been designed to focus on the following two aspects:

First, characterization of electrophysiological progression and manifestation of FeCl₃-induced post-traumatic epileptic seizures in young and old rats. Biochemical estimations and microscopic observations were performed to look for the alterations associated with FeCl₃ induced epileptogenesis. Behavioral tests were also performed to check the cognitive status of iron induced epileptogenic rats. Although, several reports are available regarding the mechanism of iron induced epileptogenesis, in the present work, however, the focus has been laid on investigating age related vulnerability to develop post-traumatic seizures. In addition, some other epileptogenesis related parameters not yet investigated or correlated with behavior were also studied in this section.

Second, investigation of antiepileptogenic efficacy of curcumin and L-deprenyl on young and old epileptic rats. Dietary intake of two different curcumin doses (500ppm and 1500ppm) was tested for both long and short term treatments. Several reports are on regarding the antioxidative properties of curcumin and its beneficial effects on neurodegenerative diseases, but the antiepileptic potential of this plant product in vivo, has hardly been investigated.

We have found that long-term treatment, both low and high dose of curcumin prevents generalization of seizures and epileptogenesis related alterations with different magnitude. However, high dose (1500 ppm) of dietary supplement of curcumin for long-term was found to be more effective in preventing epileptogenesis than short term treatment of curcumin (500 ppm). Antiepileptogenic potential of L-deprenyl has been reported in different types of epilepsy, but hardly there is any report available on its effect on post-traumatic epilepsy. We have found that long-term treatment with L-deprenyl significantly prevents progression of seizures in comparison to short-term treatment. L-deprenyl also attenuates epileptogenic alterations at biochemical, ultrastuctural and behavioral level, and was found to be less efficient than curcumin. It is apparent from study, that higher dose of L-deprenyl would be more efficacious in suppressing post-traumatic seizure if given for longer duration.
On the basis of data obtained it could be suggested that both curcumin and L-deprenyl has tendency to delay the onset and progression of post-traumatic seizures in epileptic rats. However, efficacy of curcumin to retard epileptic alterations was considerably higher in comparison to L-deprenyl. Fig-58 concludes the therapeutic targets of both curcumin and L-deprenyl.

Salient features of the investigations

1) Arrival and spread of seizures was much faster in iron injected old epileptic rats in comparison to young ones.
2) Iron induced epileptogenesis involves oxidative damage to membrane lipids and proteins in both cortex and hippocampus and results significant decline in membrane fluidity, Na-K ATPase activity and increase in PKC activity in comparison to control/saline injection.
3) Spectral analysis with the help of FFT and CWT suggests that Grade III seizures are dominated by frequencies between 6.5 to 8.0 and Grade IV seizures mainly 7-10 Hz.
4) Long-term dietary intake of curcumin counteracts iron induced epileptic alterations at both biochemical and cellular level. As both low (500) and high doses (1500 ppm) are equally effective in inhibiting epileptogenesis.

5) Higher dose of curcumin was more effective than low dose in short-term curcumin treatment.

6) Dietary intake of curcumin potentially delayed the appearance of Grade III /IV seizures in both young and old rats, indicating that curcumin has tendency to inhibit post-traumatic seizures in iron induced epilepsy.

7) Curcumin prevented biochemical alterations and protects cellular structures and degenerative changes in CA1 region.

8) L-deprenyl pretreatment significantly inhibited seizures manifestations of seizures by preventing FeCl₃ induced alterations at different levels (Biochemical, microscopic, behavioral). Observed protection of L-deprenyl is significantly less in comparison to curcumin.

9) Short-term treatment of L-deprenyl was found unable to prevent generalization of seizures completely but suppressed the seizure progression and spread. Hence, potential antiepileptogenic efficacy of higher dose of L-deprenyl in short term treatment cannot be ruled out.

10) Pearson correlation matrix between different parameters shows that all above mentioned parameters strongly correlated with each other in epileptic rats while only different biochemical parameters correlated with each other. In aging rats, weak correlation was observed in biochemical w.r.t. electrophysiological and behavioral results.

11) Correlation studies in curcumin and L-deprenyl indicates that their protective effects on electrophysiological, biochemical, histological and behavioral levels significantly correlated to each other.

Present study lead us to conclude that curcumin has antiepileptogenic potential and can be used for clinical trials for treating patients met with head trauma or patients suffering from post-traumatic seizures. Clinical reports of curcumin safe toxicity profile without any side effects are well reported in the literature. Since curcumin is extensively used as spice
in cooking food, a supplemented dose in post-traumatic patients could be of great therapeutic potential.

**Future Perspectives:**

1) Further studies need to be undertaken in order to elucidate the molecular mechanism behind the observed differential vulnerability to develop post-traumatic seizures in young and old rats.

2) Molecular and proteomic studies should be undertaken to investigate the potential therapeutic target of curcumin and L-deprenyl’s antiepileptic action.

3) For L-deprenyl, effect of higher doses need to be investigated to confirm its antiepileptogenic properties in short-term treatment.