Conclusion
Alzheimer's disease (AD) is reported to be the most common form of adult dementia (Nordberg, 1996). AD, named after Dr. Alois Alzheimer, who in 1907 published an account of rapidly deteriorating mental illness in a 51 year old women. It is a progressive and irreversible neuropsychiatric degenerative disorder of the brain with a deadly outcome that primarily affects the elderly population, and is a major public health concern. The main symptoms associated with AD involve cognitive dysfunction primarily memory loss (Kensawus, 1995). Language deficits, depression, behavioural problems including agitation, mood disturbances and psychosis are also features associated with later stages of AD.

The etiology of AD is still unknown but several factors have been suggested that appear to reduce the incidence of the disease, or for which a hypothesis has been put forward based on scientific investigations. None of the proposed theories have been completely accepted since they are largely based on epidemiological studies and other factors might be responsible for the differences observed. Nevertheless these factors have been exploited in the search of drugs to treat AD.

The pathological features that occur in the central nervous system of AD are senile plaque and neurofibrillary tangles formation, oxidative stress, inflammatory process, apoptotic cell death and neurotransmitter disturbances. A consistent neuropathological occurrence associated with memory loss is a cholinergic deficit, which has been correlated with the severity of AD (Reud, 1987; Perry, 1996). Therefore, attempts to restore cholinergic function have been a rational target for drugs used to treat the symptoms of AD. Approaches to enhance cholinergic function of AD have included stimulation of cholinergic receptors.

There is evidence supporting the hypothesis that free radicals initiate and maintain the cascade of events leading to neurodegeneration in AD. Antioxidants prophylactic/therapeutic intervention should thus disturb or prevent the free radical and amyloid beta and subsequent neurodegeneration.

At present there is no definite treatment or cure for AD. Researchers are involved in the search of some novel drugs either from herbal origin or synthetic base for the cure of AD. We have attempted to search some drugs for the prevention of AD. The drugs have shown a better protection of AD.
In a nutshell, present findings indicate that ICV-STZ treatment causes cognitive impairment, alterations in biochemical parameters, lipid peroxidation and histological changes in hippocampus in mice and rats probably by generating free radicals and depleting the acetylcholine level by altering its synthesis. Supplementation of s-allyl cysteine, rutin, taurine, and hesperidin prevented the all alteration significantly due to their antioxidant, anti-inflammatory, antiapoptotic and energy generating properties.

Rutin has shown the best results in preventing the cognitive decline, ameliorating the oxidative burdens and neuroinflammation probably by its potent antioxidant and anti-inflammatory properties and protected the brain injury subsequent to ICV-STZ injection in rats. The antioxidant and anti-inflammatory mechanisms of rutin can be understood by the Fig. 1. S-allyl cysteine and hesperidin were also found to be effective in regulating the oxidative damage and neuronal cell death in STZ model of sporadic dementia of Alzheimer’s type in mice. Taurine was also found to be effective in preventing the behavioral and biochemical parameters in ICV-STZ infused rats.

So these selected neuroprotective agents, s-allyl cysteine, rutin, taurine and hesperidin can be used as favored remedies in AD pending elucidation of proper molecular mechanisms and deciphering appropriate genetic pathways.
Chapter I: The beneficial effects of SAC in spatial memory processing may be due to its ability to maintain the cholinergic function, prevent neuronal damage possibly through its antioxidant potential. Thus these finding suggest that SAC is an alternative for preventing the cognitive impairment. Further investigation into the neuroprotective potential and mechanisms of SAC are required to determine, whether it can be an effective cure for cognitive impairment.

Chapter II: This study demonstrated that ICV-STZ causes learning and memory deficits and neuronal injury in rat hippocampus and prophylactic treatment with taurine significantly improved learning and memory deficits by inhibiting oxidative stress and ameliorating neuronal injury in hippocampus. Our results suggested that taurine is effective in ameliorating ICV-STZ induced behavioural alterations, cholinergic dysfunction and oxidative stress. Further understanding the mechanism underlying the neuroprotection of taurine may have important clinical ramifications and will provide an avenue to disclose both the pathogenesis and therapeutic mechanisms underlying current AD paradigm.

Chapter III: Our findings of this study indicate that ICV-STZ cause behavioural deficits and oxidative stress due to free radical generation and weakening the antioxidant systems. Rutin offered significant neuroprotection in ICV-STZ infused rats, which may attribute the inhibition of behavioural deficit, lipid peroxidation, inflammatory markers, PARP activity, and increase in endogenous antioxidant defence enzymes. Thus, the present study provides further evidence that rutin may be a useful intervention for the treatment of cognitive impairment. We believe that our results will contribute to the clinical applications in the treatment of sporadic dementia of Alzheimer’s type.

Chapter IV: The results from the present findings showed that ICV-STZ causes behavioural deficits along with cholinergic impairment, oxidative stress and lipid alterations in mice. Hesperidin offered significant neuroprotection in ICV-STZ infused mice, which may be attributed to inhibition of behavioural deficit, lipid per oxidation, AchE activity and augmented brain lipid content as well as GSH level. Thus, the present study provides further evidence that hesperidin may be a useful intervention for the treatment of cognitive impairment. We believe that our results will contribute to the clinical applications in the treatment of sporadic dementia of Alzheimer’s type.
References


Ansari, M.A., Joshi, G., Huang, Q., 2006. In vivo administration of D609 leads to protection of subsequently isolated gerbil brain mitochondria subjected to in vitro oxidative stress induced by amyloid beta peptide and


B


References


References


F


References


References


References

143
References


References

protective and antioxidant properties of rutin, a natural flavone, against ethanol induced gastric lesions. J. Ethnopharmacol. 71, 45-53.


Mayer, G., Nitsch, R., Hoyer, S., 1990. Effects of changes in peripheral and cerebral glucose metabolism on locomotor activity, learning and memory in adult male rats, Brain Res. 532, 95-100.


N


151


References


Qu


R


References


S


Mol. Physiol. 279, L1005–L1028.


163
Vassar, B.D., Bennett, S., Babu-Kahn, S., Kahn, E.A., Mendiz, P., Denis, D.W., Teplov, S., Ross, P.,
Beta-secretase cleavage of Alzheimer's Amyloid precursor protein by the transmembrane aspartic protease
BACE. Science. 286, 735-741.

Vayssiere, J.L., Peti, P.X., Risler, Y., Mignotte, B., 1994. Commitment to apoptosis is associated with changes
in mitochondrial biogenesis and activity in cell lines conditionally immortalized with simian virus 40. Proc. Natl.


Neuron. 44, 181-93.


Wang, J., Xiong, S., Xie, C., Markesbery, W.R., Lovell, M.A., 2005. Increased oxidative damage in nuclear and


71, 1057-1064.


Y


Z


Publications


neuroinflammation in intracerebroventricular streptozotocin injected rats. (Under review)

Conferences attended
1. Presented a paper on ‘S-allyl cysteine attenuates intracerebroventricular streptozotocin induced-memory impairment and neurodegeneration in mice’ at International conference of Indian Academy of Neurosciences, Cochin University of science and technology Cochin Kerala, India, December 12-14, 2008.

2. Presented a paper on ‘Development of rotenone induced rodent model for Parkinson’s disease’ at 1st Middle East IBRO neuroscience conference at UAE University Al-Ain UAE, Feb 7-9, 2011.