

## **Paper Six**

### **Title: N-acetylcysteine protects against cuprizone-induced demyelination: histological and immunohistochemical study**

Myelination is a sequential process that is tightly controlled by a number of intrinsic and extrinsic factors. Any CNS disease in which the neuronal myelin sheath is damaged is referred to as demyelinating disease. The present work was designed to study the histopathological, ultrastructural and immunohistochemical changes in rat brain, mainly corpus callosum (CC), following oral administration of cuprizone (CPZ), and the role of N-acetylcysteine (NAC) in reducing these changes. Demyelination was induced by CPZ administration for short (4Ws) and long (8Ws) periods. NAC was given concomitantly and sequentially for similar periods. Spontaneous recovery after cessation of CPZ followed by no medication was also investigated. At the end of each experimental period, both cerebral hemispheres were extracted and prepared for light and electron microscopic examination and immuno-histochemical study. The obtained results showed a direct proportion between the duration of CPZ administration and the severity of demyelination. The co-administration of CPZ and NAC, had a fair protective impact that was stronger than the sequential administration of the two drugs. Incomplete spontaneous remyelination was observed after cessation of CPZ, being more evident in short than in long period group, indicating that when CPZ administration is prolonged, remyelination is delayed. In the light of the above results, it could be concluded that NAC has neuroprotective effects and has the potential to be a novel therapeutic approach for the treatment of demyelinating diseases such as multiple sclerosis; however, treatment should begin as soon as the disease manifests.