The safety and efficacy assessment of *M. spinosa* and *O. indicum* to control mycotoxin (DON) induced toxicity was carried out during 2011-2015 at Defence Research Laboratory, Solmara, Tezpur, Assam.

The most sensitive indicators of acute exposure are kidney and liver. The study on the damage caused to these organs by DON is very interesting. The quantitative studies on uptake and distribution of these compounds and its processing are required to understand the acute toxicity of DON. Again, the present study revealed that DON treatment resulted in an elevation of cytotoxicity, cellular apoptosis and DNA damage which may be the cause of its cellular toxicity. Furthermore, increase of hepatocyte apoptosis was observed, indicating that DON induced hepatotoxicity may be partly mediated by apoptosis. The present data also indicated the effectiveness of DON induced hepatotoxicity *in vitro*, which inferred a possible major target other than kidney cells. This may be useful to consider human liver cells for further studies under realistic exposure concentrations for regulatory control measures of DON and DON contaminated food. DON exerts genotoxic activity as well as cytotoxic activity by induction of apoptosis. These results suggest that DON might lead to hepatocarcinogenesis by accumulation of genetic alterations. Although, in addition to that DON induced genotoxicity mechanisms will be clarified by molecular level experiments. These findings suggest that DON exert a pronounced cellular apoptosis and genotoxic effect on blood and bone marrow cells. This may be useful in planning chemotherapeutic strategy in DON toxicity. The data generated in the present study demonstrate that due to the aneugenic activity, the formation of centromere positive micronuclei increases and induction in oxidative DNA damage is caused by DON.

Furthermore, the safety performance of these two plants was evaluated using standard toxicological tests recommended as per OECD test guidelines and the test result indicated the absence of toxicity in *O. indicum* plant extracts at various doses. Interestingly, the result indicated that *M. spinosa* extract shows toxicological effect which is completely concentration dependent in comparison to *O. indicum* extract. These findings is in contradiction to the objective of the study undertaken and hence dropped *M. spinosa* for further efficacy assessment study but continued with *O. indicum* for efficacy assessment against mycotoxin induced toxicity in experimental animal model.
Chapter-6

Summary

The findings of the study revealed that the hydroalcoholic stem bark extract of *O. indicum* plant contains high levels of phenolics and flavonoids and possess significant antioxidants activities.

Moreover, the hydroalcoholic *O. indicum* stem bark extract possesses excellent hepatoprotective activity via preventing hepatic damage caused by DON-induced hepatotoxicity in mice. This protective effect may be due to antioxidant properties the extract possesses. Hence, efficacy of the hepatoprotective extract can be given on its capacity to by restoring the normal hepatic cellular physiology disturbed by a hepatotoxin (DON) and reduced harmful effects. The given plant extract showed the protective properties by regenerating the damaged liver cells and hepatocytic cell membrane structural integrity which is proven by decreased elevated levels of enzymes. Three different doses of the extract showed significant protective effects with respect to biochemical and histological parameters of hepatic injury. It is also observed that due to the presence of phenolic compounds and flavonoids, which are responsible for free radical scavenging activity showed excellent hepatoprotective response against DON induced hepatotoxicity.

As a continuation of present study, further investigations are needed to clarify the protective mechanism of *O. indicum* extract against mycotoxin induced toxicity, which may be of great pharmacological importance, and might be beneficial for cancer prevention. Furthermore, isolation and characterization of active hepatoprotective components from *O. indicum* may also be investigated in future as this plant have shown promising hepatoprotective activity. In addition, cytotoxic activity of *M. spinosa* may also be studied for achieving beneficial effect in cancer prevention.