CHAPTER 5

SUMMARY AND CONCLUSION

Both COX-1 and COX-2 have been shown to play an important role in the inflammatory response. However, the exact role and preference of COX isoform in neuroinflammation is unclear. The main objective of the study is to explore the effect of selective / non selective COX inhibitors in preventing the neuroinflammation induced by LPS. The specific objectives of the study are

- To evaluate the effect of selective and non selective COX inhibitors in LPS induced neuroinflammation in rats.

- To evaluate the mode of action of selective and non selective COX inhibitors in LPS induced neuroinflammation model in rats, and measure/ the neurochemical, biochemical and proinflammatory mediator alterations.

- To evaluate the effect of COX inhibitors in LPS induced neuronal damage, histopathological analysis is performed.

Summarizes of the findings and conclusions from the study:

- LPS 10 µg/kg was found to be effective to induce neuroinflammation in rats and this dose of LPS was finalized for further study.

- Pretreatment of aspirin was effective and based on literature reports pretreatment protocol was finalized for our further study.
• In some behavioral parameters non selective COX inhibitors showed better efficacy than selective COX inhibitors in LPS induced behavioral alterations in rats.

• Selective COX 1 inhibitor (resveratrol) and non selective COX (aspirin) inhibitor increased the antioxidant activity better than the selective COX 2 (celecoxib) inhibitor in LPS induced oxidative damage conditions.

• Non selective COX inhibitor (aspirin) attenuated the LPS induced proinflammatory mediators, neurochemical and neuroinflammation levels. This effect was found to be better than the selective COX inhibitors.

The effect of COX inhibitors has preferential activity. Among the three drugs studied non selective COX inhibitor was found to have a significant neuroprotective role than selective COX-2 though COX-2 inhibitors have been indicated as anti inflammatory drug.

Table 5.1 summarizes the effect of COX inhibitors in LPS induced changes in rats

<table>
<thead>
<tr>
<th>Parameters Evaluated</th>
<th>Non Selective COX Inhibitor (Aspirin)</th>
<th>Selective COX-1 Inhibitor (Resveratrol)</th>
<th>Selective COX-2 Inhibitor (Celecoxib)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behavior</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Learning and memory</td>
<td>++</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Proinflammatory markers</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>GABA, Glutamate and Aspartate</td>
<td>++</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Antioxidant enzymes</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Histopathological changes</td>
<td>++</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>
+ Denotes significant alteration of parameters

++ Denotes predominant effect amongst drug treatment

- Denotes no effect

The resveratrol selective COX-1 was found to be best in controlling oxidative stress. Hence we can say COX inhibitors had differential effect in controlling neuroinflammation among the studied drug aspirin and was found to be a better medicine in control of neuroinflammation induced by peripheral administration of LPS.

**Proposed mechanism of action**

![Diagram](image)

**Figure 5.1** Non selective COX inhibitor protected LPS induced neuroinflammation mediated NFκB via COX pathway