# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>CHAPTER NO.</th>
<th>TITLE</th>
<th>PAGE NO.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ABSTRACT</td>
<td>vi</td>
</tr>
<tr>
<td></td>
<td>LIST OF TABLE</td>
<td>xvi</td>
</tr>
<tr>
<td></td>
<td>LIST OF FIGURES</td>
<td>xvii</td>
</tr>
<tr>
<td></td>
<td>LIST OF SYMBOLS AND ABBREVIATIONS</td>
<td>xxii</td>
</tr>
<tr>
<td>1</td>
<td>INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>MATERIALS AND METHODS</td>
<td>11</td>
</tr>
<tr>
<td>2.1</td>
<td>Animals</td>
<td>11</td>
</tr>
<tr>
<td>2.1.1</td>
<td>Experiment 1</td>
<td>11</td>
</tr>
<tr>
<td>2.1.2</td>
<td>Experiment 2</td>
<td>13</td>
</tr>
<tr>
<td>2.1.3</td>
<td>Experiment 3</td>
<td>13</td>
</tr>
<tr>
<td>2.1.4</td>
<td>Experiment 4</td>
<td>14</td>
</tr>
<tr>
<td>2.2</td>
<td>Isolation of lymphocytes</td>
<td>15</td>
</tr>
<tr>
<td>2.3</td>
<td>Lymphocyte proliferation assay</td>
<td>15</td>
</tr>
<tr>
<td>2.4</td>
<td>Con A-induced cytokine production</td>
<td>15</td>
</tr>
<tr>
<td>2.5</td>
<td>Intracellular signaling pathway markers</td>
<td>16</td>
</tr>
<tr>
<td>2.6</td>
<td>Western blot analysis</td>
<td>16</td>
</tr>
<tr>
<td>2.7</td>
<td>Nitric oxide production</td>
<td>17</td>
</tr>
<tr>
<td>2.8</td>
<td>Hormones assays: Corticosterone and Testosterone</td>
<td>17</td>
</tr>
<tr>
<td>2.9</td>
<td>Estimation of IGF-1, BDNF and APP level</td>
<td>17</td>
</tr>
<tr>
<td>2.10</td>
<td>Cholinesterase assay</td>
<td>17</td>
</tr>
<tr>
<td>2.11</td>
<td>Antioxidant Enzyme Assays</td>
<td>18</td>
</tr>
<tr>
<td>2.11.1</td>
<td>Superoxide dismutase (SOD)</td>
<td>18</td>
</tr>
<tr>
<td>2.11.2</td>
<td>Catalase (CAT)</td>
<td>18</td>
</tr>
<tr>
<td>2.11.3</td>
<td>Glutathione Peroxidase (GPx)</td>
<td>19</td>
</tr>
<tr>
<td>2.11.4</td>
<td>Glutathione-S-transferase (GST)</td>
<td>19</td>
</tr>
<tr>
<td>2.12</td>
<td>Extent of Lipid peroxidation</td>
<td>19</td>
</tr>
<tr>
<td>2.13</td>
<td>Protein carbonyl formation</td>
<td>19</td>
</tr>
</tbody>
</table>
3 ESTABLISHMENT OF DOSE RESPONSE OF *MORINDA CITRIFOLIA* FRUIT JUICES (NFJ, NSL, NWS) ON LYMPHOPROLIFERATION AND ANTIOXIDANT ENZYMES IN SPLENIC LYMPHOCYTES OF YOUNG MALE WISTAR RATS

3.1 Rationale
3.2 Treatment
3.2.1 Experiment
3.3 Results
3.3.1 Effects of Noni (*Morinda citrifolia*) fruit juice (NFJ), Noni fruit juice with seed (NWS) and Noni seedless fruit juice (NSL) on lymphocyte proliferation
3.3.2 Effects of Noni (*Morinda citrifolia*) fruit juice (NFJ), Noni fruit juice with seed (NWS) and Noni seedless fruit juice (NSL) on antioxidant enzyme activities and extent of lipid peroxidation
3.3.2.1 Superoxide dismutase (SOD)
3.3.2.2 Catalase (CAT)
3.3.2.3 Glutathione Peroxidase (GPx)
3.3.2.4 Extent of lipid peroxidation
3.4 Discussion
3.5 Key Findings

4 SELECTIVE MODULATION OF AGE-ASSOCIATED IMMUNE FUNCTION AND ANTIOXIDANT ENZYME ACTIVITIES BY PHYTOCHEMICALS IN *MORINDA CITRIFOLIA* FRUIT THROUGH ERK PATHWAY IN SPLENOCYTES OF MALE F344 RATS

4.1 Rationale
4.2 Treatment
4.2.1 Experiment 1
4.2.2 Experiment 2: Docking

4.3 Results

4.3.1 Effects of Noni seedless fruit juice (NSL) and Noni fruit juice with seed (NWS) on age-related proliferation of splenocytes

4.3.2 Effects of Noni seedless fruit juice (NSL) and Noni fruit juice with seed (NWS) on age-related cytokine production

4.3.3 Effects of Noni seedless fruit juice (NSL) and Noni fruit juice with seed (NWS) on age-related cellular antioxidant status

4.3.4 Effects of NSL and NWS on age-related expression of p-ERK/Total ERK, p-CREB/Total CREB, and p-Akt/Total Akt in splenocytes

4.3.5 NSL treatment enhanced p-NF-κB (p50) expression in young rats although decreased p-NF-κB (p50) expression in middle-aged and old rats

4.3.6 NWS treatment enhanced p-NF-κB (p50) expression in young rats, middle-aged and old rats

4.3.7 Docking of ERK by known Noni phytochemicals—Damnacanthal, myricetin and ursolic acid

4.4 Discussion

4.5 Key Findings

5 MORINDA CITRIFOLIA FRUIT JUICE FACILITATES THE MODULATION OF NEURAL-IMMUNE INTERACTIONS IN THE SPLEEN OF F344 MALE RATS

5.1 Rationale

5.2 Treatment

5.2.1 Experiment

5.2.1.1 Experiment 1

5.2.1.2 Experiment 2
5.3 Results

5.3.1 Effect of oral administration of Noni \textit{(Morinda citrifolia)} fruit juice on body weight of F344 rats

5.3.2 Treatment with Noni \textit{(Morinda citrifolia)} fruit juice treatment enhanced Con A-induced splenocytes proliferation

5.3.3 Treatment with Noni \textit{(Morinda citrifolia)} fruit juice increased cell-mediated immune function

5.3.4 Effects of Noni \textit{(Morinda citrifolia)} fruit juice on the expression of p-TH, NGF, p-mTOR, p-I\kappa B-\alpha and p-NF-\kappa B (p50 and p65)

5.3.5 Effects of Noni \textit{(Morinda citrifolia)} fruit juice on age-related expression of p-ERK/Total ERK, p-CREB/Total CREB, and p-Akt/Total Akt in splenocytes

5.3.6 Treatment with Noni \textit{(Morinda citrifolia)} fruit juice decreased the extent of lipid peroxidation

5.3.7 \textit{In vivo} treatment with Noni \textit{(Morinda citrifolia)} fruit juice down-regulated the protein carbonyl formation

5.3.8 \textit{In vivo} treatment with Noni \textit{(Morinda citrifolia)} fruit juice increased nitric oxide (NO) production

5.4 Discussion

5.5 Key Findings

6 EFFECTS OF \textit{MORINDA CITRIFOLIA} FRUIT JUICE ON THE MODULATION OF GROWTH FACTORS AND CHOLINERGIC ACTIVITY IN DIFFERENT BRAIN AREAS OF OLD F344 RATS

6.1 Rationale

6.2 Treatment

6.2.1 Experiment

6.3 Results
6.3.1 Effects of Noni (*Morinda citrifolia*) fruit juice on serum corticosterone and testosterone levels in old F344 rats

6.3.2 Treatment with Noni (*Morinda citrifolia*) fruit juice decreased APP levels in FC, STR, MBH and HP

6.3.3 Treatment with Noni (*Morinda citrifolia*) fruit juice increased BDNF levels in FC and HP

6.3.4 Treatment with Noni (*Morinda citrifolia*) fruit juice increased the IGF-1 levels in FC, STR, MBH and HP

6.3.5 Treatment with Noni (*Morinda citrifolia*) fruit juice on the expression of p-ERK/Total ERK, p-CREB/Total CREB and p-Akt/Total Akt in the brain areas of old F344 rats

6.3.5.1 Frontal cortex

6.3.5.2 Striatum

6.3.5.3 Medial basal hypothalamus

6.3.5.4 Hippocampus

6.3.6 Treatment with Noni (*Morinda citrifolia*) fruit juice augmented NO production in the FC, STR, and HP

6.3.7 Treatment with Noni (*Morinda citrifolia*) fruit juice decreased butyryl cholinesterase (BChE) activity in serum and total cholinesterase (TChE) activity in MBH and HP

6.4 Discussion

6.5 Key Findings

7 CONCLUSION

REFERENCES

APPENDICES

A1. Effects of Noni (*Morinda Citrifolia*) fruit juice (NFJ) on antioxidant enzymes activities and
extent of lipid peroxidation on various brain areas [frontal cortex (FC), medial basal hypothalamus (MBH), striatum (STR), and hippocampus (HP)] of old F344 rats

**A1.1** Superoxide dismutase (SOD) 111

**A1.2** Catalase (CAT) 112

**A1.3** Glutathione peroxidase (GPx) 113

**A1.4** Glutathione-S-transferase (GST) 114

**A1.5** Extent of lipid peroxidation (TBARS) 115

**LIST OF PUBLICATIONS** 116

**VITAE** 117