# INDEX

<table>
<thead>
<tr>
<th>Section</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACKNOWLEDGEMENT</td>
<td>i-ii</td>
</tr>
<tr>
<td>ABBREVIATIONS</td>
<td>iii-iv</td>
</tr>
<tr>
<td><strong>1</strong> INTRODUCTION</td>
<td></td>
</tr>
<tr>
<td>1.1 General</td>
<td>1-2</td>
</tr>
<tr>
<td>1.2 Pesticides: Types, Uses and Hazards</td>
<td>2-5</td>
</tr>
<tr>
<td>1.3 Global perspective</td>
<td>5-6</td>
</tr>
<tr>
<td>1.4 Indian scenario</td>
<td>6</td>
</tr>
<tr>
<td>1.5 Pesticide toxicity</td>
<td>7-8</td>
</tr>
<tr>
<td>1.6 Mode of action of OP pesticides</td>
<td>8-11</td>
</tr>
<tr>
<td>1.7 Oxidative stress and redox imbalance</td>
<td>11-12</td>
</tr>
<tr>
<td>1.8 Genotoxicity, carcinogenicity and mutagenicity</td>
<td>12-13</td>
</tr>
<tr>
<td>1.9 Therapeutic role of antioxidants</td>
<td>13-14</td>
</tr>
<tr>
<td>1.10 Aims and Objectives</td>
<td>14-15</td>
</tr>
<tr>
<td><strong>2</strong> REVIEW OF LITERATURE</td>
<td></td>
</tr>
<tr>
<td>2.1 General</td>
<td>16-21</td>
</tr>
<tr>
<td>2.2 Neurotoxicity and other toxic effects</td>
<td>21-23</td>
</tr>
<tr>
<td>2.3 Biotransformation of organophosphate pesticides and susceptibility to pesticides exposure</td>
<td>24-26</td>
</tr>
<tr>
<td>2.4 Pesticide induced oxidative stress and redox imbalance</td>
<td>26-30</td>
</tr>
<tr>
<td>2.5 Pesticide induced DNA damage, genotoxicity and mutagenicity</td>
<td>30-34</td>
</tr>
<tr>
<td>2.6 Consequences of DNA damage</td>
<td>35-37</td>
</tr>
<tr>
<td>2.7 Pesticide induced changes in DNA repair</td>
<td>37-40</td>
</tr>
<tr>
<td>2.8 Pesticides and Epigenetics</td>
<td>40-44</td>
</tr>
<tr>
<td>2.9 Diagnosis, management and treatment of OP pesticide exposure</td>
<td>44-49</td>
</tr>
<tr>
<td>2.10 Expected outcome and future prospects of the present study</td>
<td>49-51</td>
</tr>
</tbody>
</table>
MATERIALS & METHODS

3.1 Studies on monocrotophos and quinalphos induced changes in the redox status of rat tissues and protective effects of antioxidant vitamins

3.1.1 Chemical
3.1.2 Study design
3.1.3 Acute exposure
3.1.4 Chronic exposure
3.1.5 Estimation of reduced and oxidized glutathione
3.1.6 Estimation of NADP⁺, NADPH, NAD⁺ and NADH
3.1.7 Glutathione reductase (GR, E.C.No.1.6.4.2)
3.1.8 Glucose-6-phosphate dehydrogenase (G6PDH, E.C.No.1.1.1.49)
3.1.9 Studies on gene expression
3.1.9.1 Preparation of glassware
3.1.9.2 RNA isolation
3.1.9.3 Reverse transcriptase polymerase chain reaction
3.1.9.4 DNA electrophoresis and observation
3.1.9.5 Normalization of results
3.1.10 Protein estimation
3.1.11 Statistical analyses

3.2 Evaluation of genotoxicity of monocrotophos and quinalphos in rats and protective effects of melatonin

3.2.1 Chemicals
3.2.2 Study design
3.2.3 Acute exposure
3.2.4 Chronic exposure
3.2.5 Isolation of lymphocytes
3.2.6 Single cell gel electrophoresis (SCGE) or Comet assay
3.2.7 Micronucleus assay
3.2.8 DNA-protein crosslinks
3.2.9 Statistical analyses
3.3 Studies on monocrotophos and quinalphos induced oxidative DNA damage in rat tissues and lymphocytes

3.3.1 Chemicals
3.3.2 Study design
3.3.3 Acute exposure
3.3.4 Chronic exposure
3.3.5 Estimation of superoxide anion
3.3.6 Estimation of hydrogen peroxide
3.3.7 Estimation of malondialdehyde and 4-hydroxynonanal
3.3.8 Estimation of total antioxidant capacity
3.3.9 Estimation of damaged bases and DNA single strand breaks
3.3.10 Statistical analyses

3.4 Studies on monocrotophos and quinalphos induced oxidative damage of bases, status of the repair enzymes and epigenetic changes in rat tissues

3.4.1 Chemicals
3.4.2 Study design
3.4.3 Acute exposure
3.4.4 Single cell gel electrophoresis (SCGE) or comet assay
3.4.5 Estimation of total antioxidant capacity
3.4.6 Studies on expression of genes of DNA repair enzymes
3.4.6.1 Preparation of glassware
3.4.6.2 RNA isolation
3.4.6.3 Reverse transcriptase polymerase chain reaction
3.4.6.4 DNA electrophoresis and observation
3.4.6.5 Normalization of results
3.4.7 Studies on DNA methylation
3.4.8 Statistical analyses
RESULTS AND DISCUSSION

4.1 Studies on the effect of MCP and QNP exposure, singly and in combination on the redox status and glutathione regenerating enzymes in rat tissues and protective effects of antioxidant vitamins

4.1.1 Effect of acute and chronic exposure of MCP and QNP on the levels of GSH, GSSG, and GSH/GSSG ratio.

4.1.2 Effect of acute and chronic exposure of MCP and QNP on the levels of NAD⁺, NADH, NADH/NAD⁺, NADP⁺, NADPH, and NADPH/NADP⁺ ratio.

4.1.3 Effect of acute and chronic exposure of MCP and QNP on the activities of glutathione reductase and glucose-6-phosphate dehydrogenase and their expression.

Discussion

4.2 Studies on the effect of MCP and QNP exposure, singly and in combination on DNA damage and DNA protein crosslinks in rat tissues and lymphocytes and protective effects of melatonin

4.2.1 Effect of acute exposure of MCP and QNP on DNA strand breaks and protective effects of melatonin

4.2.2 Effect of chronic exposure of MCP and QNP on DNA strand breaks and protective effects of melatonin

4.2.3 Effect of acute exposure of MCP and QNP on micronuclei induction in polychromatic erythrocytes and protective effects of melatonin

4.2.4 Effect of chronic exposure of MCP and QNP on micronuclei induction in polychromatic erythrocytes and protective effects of melatonin

4.2.5 Effect of acute and chronic exposure of MCP and QNP on DNA protein crosslink formation in rat lymphocytes and protective effects of melatonin

Discussion

4.3 Studies on monocrotophos and quinalphos induced oxidative DNA damage in rat tissues and lymphocytes

4.3.1 Estimation of lipid peroxidation

4.3.2 Estimation of total antioxidant capacity

4.3.3 Estimation of superoxide anion

4.3.4 Estimation of levels of hydrogen peroxide

4.3.5 Study of the dose dependent toxicity of MCP and QNP singly and in combination
combination and co-treatment of melatonin in terms of DNA damage
Discussion

4.4

Studies on the effect of MCP and QNP exposure on the expression of
enzymes of base excision repair and DNA methylation

4.4.1

Effect of MCP and QNP exposure on the levels of single strand and
double strand breaks one day and five days post exposure

4.4.2

Alterations in the expression of DNA repair enzymes on MCP and QNP
exposure in rat tissues

4.4.3

Effect of MCP and QNP exposure on DNA methylation in rat tissues

4.4.4

Effect of MCP and QNP exposure on the total antioxidant capacity

4.4.5

Discussion

SUMMARY AND CONCLUSIONS

5.1

Studies on the effect of MCP and QNP exposure, singly and in
combination on the redox status, and glutathione regenerating
enzymes in rat tissues and protective effects of antioxidant vitamins.

5.2

Studies on the effect of MCP and QNP exposure, singly and in
combination on DNA damage and DNA protein crosslinks in rat tissues
and lymphocytes and protective effects of melatonin.

5.3

Studies on the effect of MCP and QNP exposure, singly and in
combination on the generation reactive oxygen species, lipid
peroxidation and damage of purine and pyrimidine bases in rat tissues
and lymphocytes and protective effects of melatonin.

5.4

Studies on the effect of MCP and QNP exposure on the expression of
enzymes of base excision repair and DNA methylation.

Conclusions

BIBLIOGRAPHY

PUBLICATIONS