The present study was carried out to evaluate the effect of curcumin on lipid peroxidation and antioxidant levels in DMBA (7, 12 Diemthyl Benanthracene) induced mammary carcinogenesis in rats. Twenty four Sprague-Dawley rats were equally distributed to control, DMBA, Tamoxifen (Standard drug) and curcumin groups. DMBA group showed significant (P<0.05) increase in lipid peroxidation and antioxidants superoxide dismutase (SOD) and catalase (CAT) levels besides reduced glutathione (GSH). Whereas, curcumin and Tamoxifen treated groups did not show any significant difference in lipid peroxidation and antioxidant status when compared to the control. Selective growth advantage of tumour cells was evident in the DMBA group and curcumin was able to prevent lipid peroxidation.

Keywords: Antioxidant, curcumin, DMBA, lipid peroxidation, mammary carcinogenesis

INTRODUCTION

Appropriate levels of reactive oxygen species (ROS) play an important role in the modulation of several physiologic responses, as ROS are part of a signaling network regulating cell function. But, an abnormal regulation of ROS has a role in pathological conditions, including inflammation, atherosclerosis, angiogenesis, aging and cancer. The mitochondrial respiratory chain is one of the major sources of endogenous ROS, together with other oxidative enzymes, such as plasma membrane oxidases (Lambeth, 2004). Curcumin is a dietary antioxidant derived from turmeric (Curcuma longa, Zingiberaceae) and has been known since ancient times to possess therapeutic properties. It has been reported to scavenge oxygen free radicals and to inhibit lipid peroxidation, acting in the protection of cellular macromolecules, including DNA, from oxidative damage (Antunes et al., 2000). Hence, an attempt was made to study the antioxidant potential of curcumin in experimental mammary carcinogenesis in rats.

MATERIALS AND METHODS

Twenty four virgin female (IAEC approval-1831/E/DFBS/IAEC/2010 dated 24.06.2011), 40-days-old Sprague-Dawley rats obtained from National Institute of Nutrition, Hyderabad were acclimatised for 5 days and were randomised and equally (n=18) distributed to four groups based on their body weight (g). The experiment was started from 45th day of age. Group 1 is control. Group 2
(DMBA) was administered with 5 mg of DMBA in olive oil/animal/week/per os for 4 weeks. Group 3 was DMBA+tamoxifen. Group 4 was DMBA+curcumin. Tamoxifen was administered in corn oil at a dose rate 100 mg/kg BW/day/per os. Curcumin (Procured from M/s. Natural Remedies Private Limited, Bengaluru, India [Batch No. PC/CL/10LOT09] stored at room temperature) was dissolved in 0.5 per cent methyl cellulose and administered orally at the dose rate of 2 g/kg BW/Week till the end of 16 week study.

In the DMBA group, out of 32 tumours recorded in 15 animals, nine were benign tumours and 23 were adenocarcinomas. In the tamoxifen group, out of 10 tumours recorded in four were benign tumours and six were adenocarcinomas. In the curcumin group, out of eight tumours recorded in four animals three were benign tumours and five were adenocarcinomas. Normal and malignant mammary tumour (Curcumin group one benign tumour) samples (n=6) were collected in sterile normal saline for lipid peroxidation and antioxidant profile. Tissue protein was estimated by the method of Lowry et al. (1951). Glutathione peroxidase (GPx) was measured by the method of Rotruck et al. (1973). Superoxide dismutase (SOD) was measured by the method of Marklund and Marklund (1974). Reduced glutathione (GSH) were estimated by the method of Meron et al. (1979). Lipid peroxidation (MDA) assay was determined as thiobarbituric acid reactive substances (TBARs) by the method of Yagi (1976). Catalase (CAT) was assayed by the method of Caliborne (1985). The data generated from different parameters of the experimental study were subjected to one-way analysis of variance (ANOVA) test using SPSS software version 20 for windows.

RESULTS AND DISCUSSION

Mean (±SE) lipid peroxidation and antioxidant values of DMBA induced mammary tumour in tamoxifen and curcumin treated Sprague-Dawley rats are presented in Table 1. No significant difference was observed in the mammary tumour tissues from tamoxifen and curcumin treated groups for lipid peroxidation compared to that of the control group. Significant (P<0.05) increase was noticed in lipid peroxidation and the levels of CAT, SOD and GSH in the mammary tumour tissues of DMBA group when compared to that of the control. There was a significant (P<0.05) decrease in the GPx value of the DMBA group when compared to the other groups.

In the present study, the DMBA group showed increased lipid peroxidation and increased levels of antioxidants except GPX which was in accordance with the findings of Kumaraguruparan et al. (2002 and 2005) and Kujur et al. (2009) who suggested that increased lipid peroxidation and host antioxidant defences associated with the development of breast cancer might offer a selective growth advantage to tumour cells over their surrounding normal counterparts. Cancer cells with increased activities of antioxidants are presumed to escape recognition by cytotoxic lymphocytes (Lu et al., 1997).

On lipid peroxidation, increased generation of oxygen free radicals induce SOD and CAT which play a key role in the detoxification of superoxide anion and hydrogen peroxide. Obrador et al. (1997) documented that glutathione, an important substrate for GPx and Glutathione-S-transferase had regulatory effect on cell
proliferation and GSH synthesis in tumour tissues was found to be associated with a high rate of cell proliferation. In this study, increase in GSH and decrease in GPx supported tumour growth in the DMBA treated group. The increase in lipid peroxidation was counterbalanced by enhanced host antioxidant defence systems protecting against oxidative stress. Halliwell (2000) suggested that oxidative stress could cause upregulation of antioxidant enzymes that rendered cells more resistant to subsequent oxidative insult.

Whereas, curcumin having polyphenolic structure and â-diketone functional groups inhibits peroxidation of membrane lipids and maintains cell membrane integrity and their function (Balasubramanyam et al., 2003). Singletary et al. (1998) reported that curcumin is a potent inducer of detoxifying enzymes and thereby prevents the toxicity induced by a chemical carcinogen. Curcumin and tamoxifen treatment may stabilize the cell membrane and significantly reduce the extent of lipid peroxidation and thereby there is no increase in the antioxidant levels in the both the treatment groups when compared to the control group.

DMBA treatment showed increased lipid peroxidation and enhanced host antioxidant defence mechanism showing selective growth advantage of tumour cells in rat experimental mammary carcinogenesis. Whereas, curcumin and tamoxifen groups inhibited lipid peroxidation and oxidative stress with no increase in the antioxidant levels when compared with the control group.

Table – 1

Mean (± SE) lipid peroxidation and antioxidant values of DMBA induced mammary tumour in tamoxifen and curcumin treated Sprague-Dawley rats (n = 6)

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Group</th>
<th>Lipid peroxidation</th>
<th>CAT</th>
<th>SOD</th>
<th>GSH</th>
<th>GPx</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Control</td>
<td>172.93± 1.65</td>
<td>0.94±0.14</td>
<td>132.15±1.31</td>
<td>195.50±3.94</td>
<td>9.72±0.62</td>
</tr>
<tr>
<td>2.</td>
<td>DMBA</td>
<td>301.57± 4.50</td>
<td>1.80±0.17</td>
<td>209.59±2.54</td>
<td>804.47±3.31</td>
<td>5.40±0.68</td>
</tr>
<tr>
<td>3.</td>
<td>Tamoxifen</td>
<td>177.23± 2.50</td>
<td>1.08±0.20</td>
<td>133.40±1.89</td>
<td>204.78±3.73</td>
<td>8.06±0.40</td>
</tr>
<tr>
<td>4.</td>
<td>Curcumin</td>
<td>174.65± 2.23</td>
<td>0.94±0.17</td>
<td>134.62±1.59</td>
<td>196.41±1.22</td>
<td>8.00±0.52</td>
</tr>
</tbody>
</table>

Means with same superscripts within a column do not differ from each other (P<0.05).

GSH - mg/g of tissue, CAT - im of H₂O₂ decomposed/min/mg protein, SOD - enzyme required to inhibit 50% pyrogallol autoxidation/min/mg protein, GPx - im of glutathione utilized/min/mg protein, TBARs - nm of MDA/g of tissue, TP - mg/g tissue.

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REFERENCES


