Antitumor and Antioxidant Activity of *Capparis sepiaria* Against Dalton’s Ascites Lymphoma in Rodents

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**Abstract:** The methanol extract of *Capparis sepiaria* (Capparaceae) bark (MECS) were evaluated for antitumor activity and antioxidant activity against Dalton’s ascites lymphoma (DAL)-bearing Swiss albino mice. The extract was administered at the doses of 200 and 400 mg/kg body weight per day for 14 days after 24 h of tumor inoculation. After the last dose and 18 h fasting, the mice were sacrificed. The present study deals with the effect of MECS on the growth of transplantable murine tumor, life span of DAL-bearing hosts, hematological profile, biochemical and antioxidant profile. MECS caused significant decrease in tumor volume, packed cell volume and viable cell count; and it prolonged the life span of DAL-tumor bearing mice. Hematological profile converted to more or less normal levels in extract-treated mice. The lipoperoxidation was increased in tumor bearing animals, after treatment with MECS antioxidant levels increased significantly. The results indicate that MECS exhibited significant antitumor activity in DAL-bearing mice.

**Key words:** Oxidative stress · Transplantable tumors · Anticancer · Dalton’s ascites lymphoma · *Capparis sepiaria* · Antitumor

**INTRODUCTION**

Cancer is the uncontrolled growth of abnormal cells in the body. This results from a series of molecular events that fundamentally alter the normal properties of cells. In cancer cells the normal control systems that prevent cell overgrowth and the invasion of other tissues are disabled. These altered cells divide and grow, display uncontrolled growth, invasion and sometimes metastasis. According to a study by the World Health Organization, one in 12 women in urban India will develop cancer in their lifetime. Approximately 40 per cent of new cases of cancer in India afflict women. Cancer is one of the leading cause to death in the developed and developing countries [1]. Cancer accounted for 7.1 million deaths in 2003 and it is estimated the overall number of new cases will rise by 50% in the next 20 years [2].

Experimental tumor models have a wide role in anticancer drug discovery. A Dalton’s ascites lymphoma (DAL) tumorigenesis model in Balb/c / Swiss albino mice provides a convenient model system to study antitumor activity within a short time [3]. Following transplantation of DAL cells into the abdominal cavity of healthy recipient mice, tumorigenesis begins immediately and aggressively [4, 5]. Free radicals are the chemical species contains at least one ‘unpaired of electron’. Reactive oxygen species (ROS) are the free radicals associated with the oxygen atom or their equivalents and have stronger reactivity with other molecules than with molecular oxygen (O$_2$). ROS usually indicate the major following four species: (i). Superoxide anion radical (O$_2^-$); (ii) hydrogen peroxide (H$_2$O$_2$); (iii) hydroxyl Radical (OH); and (iv). Singlet oxygen (O$_1^-$). (H$_2$O$_2$) and (O$_1^-$) are not free radicals by definition but they behave like free radicals.

Free radicals are implicated in many pathological conditions by irreversibly damaging the structure of biological molecules like cell membranes, DNA, Proteins etc. These free radicals can directly interacting with DNA produce single or double strand DNA breaks, DNA cross linking, purine, pyrimidine, or deoxyribose modifications and DNA cross-links. Persistent DNA damage can result in either arrest or induction of transcription, induction of signal transduction pathways, replication errors and genomic instability, all of which to cancer [6].

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Plants are the rich source of medicines from ages. They produce bioactive molecules which can be used to ameliorate various types of disorders. Over the last few decades there has been increased interest by pharmaceutical industries to discover the new drugs from the ethnomedicinal plants to provide new and alternative drugs to synthetic drugs for treatment of dreadful diseases. Potent anticancer drugs like taxol, vinblastine, vincristine, the camptothecin derivatives, topotecan and irinotecan are derived from plant sources and they are in efficient clinical use.

Many species of *Capparis* are reported from India and different parts of the world. *Capparis sepiaria* is widely distributed in India, Sri Lanka, Mayanmar and Pakistan. It is a climbing shrub with curved thorns, elliptical leaves and simple flowers, fruits are in clusters, pisiform and black. It is distributed throughout salty ranges of Andhra Pradesh, Maharashtra and Karnataka. Ethnomedicinal studies are stating that *C. sepiaria* used as blood purifier, stomachic, tonic and appetizer [7, 8]. Its flowers, leaves and roots are used in cough and toxaemia and root powder is also used as a cure for the snake bite. It is also possesses febrifuge properties and also used to treat skin diseases, tumors and diseases of muscles. Various bioactive compounds can be seen in *Capparis sepiaria* like alkaloids, phenols, sterols or glycosides. β-sitosterol, present in whole plant and leaf extract of *C. sepiaria*. Betulin is also identified from whole plant and leaf extracts. Leaf contains a, β-amyrin, taraxasterol, erythrodiol, whole plant n-octacosanol [9]. Extracts of different parts of *Capparis* show biological activities against various diseases. *C. sepiaria* seed have been considered as antidote for snake bite. Root can be used in earache and mumps. Stem root bark having therapeutic value in curing dropy gout, aphthae. This further suggests that *Capparis species* roots might have chemical compound with anticancer properties as well, which requires standardization.

The authors studied the antitumor activity of *C. sepiaria* against Dalton’s ascitic lymphoma in rodents. The aim of the present study to evaluate the antitumor activity of the methanolic extract of bark of *C. sepiaria* against Dalton’s ascitic lymphoma.

**MATERIALS AND METHODS**

**Plant Material:** The plant *C. sepiaria* (Family: Capparaceae) was collected in the month of October 2011. from the Talakona forest, Chittor district. The plant material was taxonomically identified by the taxonomist, S.V University, Tirupathi. The dried powder material of the bark of the *C. sepiaria* was extracted with methanol (yield 14.5%) in a soxhlet apparatus. The methanol extract was then distilled, evaporated and dried in vacuum. Preliminary qualitative analysis of the methanol extract showed the presence of alkaloid, tannin, saponins, reducing sugar and triterpenes. The methanol extract of *C. sepiaria* (MECS) was used for the present study.

**Experimental Animals:** The study was carried out after obtaining permission from Institutional animal ethics committee (No. 160/SPIPS/Wgl/IAEC/2011) and CPCSEA regulations were adhered to during the study. Male swiss albino mice (20-25 g) were selected for this study. The animals were maintained under standard environmental conditions and fed with standard pellet feed and water *ad libitum*.

**Tumor Cells:** DAL cells were obtained from Amala Cancer Institute, Thrissur, Kerala, India. The DAL cells were maintained by intraperitoneal inoculation of 2×10⁶ cells/mouse. Ascitic fluid was drawn out from DAL tumor bearing mouse at the log phase (days 10-12 of tumor bearing) of the tumor cells. Each animal received 0.2 ml of tumor cell suspension containing 2×10⁶ tumor cells intraperitoneally.

**Treatment Schedule:** 60 male Swiss albino mice were divided into five groups (n = 10) and given food and water *ad libitum*. All the animals in each groups except Group-I received DAL cells (2×10⁶ cells/mouse i.p.). This was taken as day ‘0’. Group-I served as normal control (25% Tween 80 per oral) and Group-II served as DAL control. 24-h after DAL transplantation, Group-III and Group-IV received methanol extract of *C. sepiaria* (MECS) at a dose of 200 and 400 mg/kg/oral for 14 consecutive days, respectively. Group-V received reference drug 5-fluorouracil (20 mg/kg oral) for 14 consecutive days [10]. 24 hours of last dose, 5 animals of each group were sacrificed to study the tumor growth parameters (mean survival time, viable, non-viable cell, tumor volume, tumor weight and tumor packed cell volume), antioxidant and hematological parameters and the rest were kept with food and water *ad libitum* to check percentage increase in life span of the tumor host.

**In Vitro-Cytotoxicity Study:** DLA cells (1×10⁶ in phosphate buffer saline (PBS) and different concentrations (50, 100, 200, 400, 600, 800, 1000, 1600 ug/ml) of MECS were incubated at 37°C for 3 hrs in 5%
CO₂ atmosphere in the filtered cap, flat bottom cell culture flasks. The viability of cells was determined by Trypan Blue dye exclusion method [11].

\[
\% \text{ cell viability} = \frac{\text{No. of Dead cells}}{\text{No. of viable cells} + \text{No. of dead cells}} \times 100
\]

**Tumor Growth Parameters**

**Tumor Volume and Weight:** After 14 days of treatment, mice were dissected and the ascitic fluid was collected from peritoneal cavity. The volume was measured by taking it in a centrifuge tube and weighed immediately [12].

**Viable and Non-Viable Tumor Cell Count:** The viability and nonviability of the cell were checked by trypan blue dye exclusion assay. The cells were stained with trypan blue (0.4% in normal saline) dye. Live (viable) cells actively pump out the dye by efflux mechanism where as dead (non-viable) cells do not. The number of viable and nonviable cells was counted [13].

\[
\text{Cell count} = \frac{\text{Number of cells} \times \text{dilution factor}}{\text{Area} \times \text{thickness of liquid film}}
\]

**Tumor Packed Cell Volume:** The ascitic fluid was collected into Wintrobe’s tube and it was centrifuged at the rate of 3000 rpm for a period of one hour. The volume of packed cells read directly as percentage [14].

**Percentage Increased in Life Span:** The effect of MECS on percentage increases in life span was calculated on the basis of mortality of the experimental mice [14].

\[
\text{ILS} (%) = \left( \frac{\text{Mean survival time of the treated group}}{\text{Mean survival time of the control group}} - 1 \right) \times 100
\]

\[
\text{Mean survival time} = \frac{\text{First death} + \text{last death}}{2}
\]

* Time denoted by days

**Hematological Parameters:** At the end of the experimental period, blood was collected from retroorbital plexuses and used for the estimation of hemoglobin (Hb) content, red blood cell (RBC) count, white blood cell (WBC) count, packed cell volume (PCV) and differential count [15, 16, 17] by standard procedures.

**Biochemical Parameters:** The remaining blood was centrifuged and serum was used for the estimation of liver biochemical parameters like Serum glutamic pyruvic transaminase (SGPT), Serum glutamic oxaloacetic transaminase (SGOT), Albumin, Total protein (TP), Total bilirubin, Alkaline phosphatase, Gamma-glutamyl transpeptidase (GGT) [18].

**Antioxidant Activity:** The liver was excised, rinsed in ice cold normal saline followed by cold 0.15M Tris-Hcl (pH 7.4), blotted and weighed. The homogenate was processed for estimation of Lipid peroxidation (LPO) [19], Superoxide Dismutase (SOD) [20], Catalase (CAT) [21], Reduced glutathione (GSH) [22], Glutathione peroxidase (GPx) [23], Glutathione-S-Transferase (GST) [24].

**Effect of on Normal Peritoneal Cell Count:** To evaluate effect of MECS on normal peritoneal cells, 3 groups of normal mice (n = 4) were taken. One group was treated with 400 mg/kg p.o. of MECS and the second group received the same treatment for 2 consecutive days. The untreated third group was used as control. Peritoneal exudate cells were collected after 24 h treatment by repeated intraperitoneal wash with normal saline and counted in each of the treated groups and compared with those of the untreated group [25].

**Effect of on Solid Tumor:** Mice were divided into two groups (n = 4). DAL cell lines (1x10⁶ cells/mice) were injected into right hind limb (thigh) of all mice intramuscularly. The Group I used as DAL tumor control. The Group II treated with MECS 400 mg/kg/oral for 14 days. Tumor mass was measured from 15th day of tumor induction. The measurement was carried out every 5th day for a period of 30 days. Tumor mass volume was measurement using following formula \(V=\frac{4}{3}\pi r^3\), where \(r\) is the mean of \(r_1\) and \(r_2\) which are two independent radii of the tumor mass [26].

**Statistical Analysis:** All data are expressed as mean ± S.E.M. Statistical significance (\(p\)) calculated by ANOVA followed by Dennett’s (tumor volume, tumor weight, viable, non viable, mean survival time, tumor PCV) and Benferroni tests (hematological, SGPT, SGOT, Total Protein, albumin, Antioxidant parameters). \(p<0.05\) was considered as statistically significant.

**RESULTS**

**In Vitro-Cytotoxicity Study:** The In vitro cytotoxicity effect of MECS at various concentrations 50, 100, 200, 400, 600, 800, 1000, 1600 µg/ml on DAL cell lines using tryphan blue dye exclusion assay method has shown in the
Table 1: Effect of methanol extract of *Capparis sepiaria* on tumor growth parameters:

<table>
<thead>
<tr>
<th>Parameters</th>
<th>DAL</th>
<th>DAL + MEDP 200 mg/kg</th>
<th>DAL + MEDP 400 mg/kg</th>
<th>DAL + 5-FU 20 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean survival time (days)</td>
<td>13.5±0.96</td>
<td>19.2±0.58</td>
<td>22.5±2.24*</td>
<td>25.6±2.06**</td>
</tr>
<tr>
<td>Increased life span (%)</td>
<td>---</td>
<td>31</td>
<td>46*</td>
<td>61*</td>
</tr>
<tr>
<td>Tumor volume (ml)</td>
<td>18±2.4</td>
<td>11.4±2.08**</td>
<td>4.7±0.91***</td>
<td>4.8±1.29***</td>
</tr>
<tr>
<td>Tumor packed cell volume (ml)</td>
<td>51.12±2.9</td>
<td>33.61±2.9**</td>
<td>36.7±1.7**</td>
<td>31.6±1.7**</td>
</tr>
<tr>
<td>Viable cell count (x10^6/mg)</td>
<td>18.63±0.96</td>
<td>17.91±0.83*</td>
<td>12.48±0.7**</td>
<td>12.65±0.68**</td>
</tr>
<tr>
<td>Nonviable cell count (x10^6/mg)</td>
<td>0.17±0.017</td>
<td>0.25±0.02*</td>
<td>0.52±0.04**</td>
<td>0.71±0.06**</td>
</tr>
</tbody>
</table>

Data are expressed as the mean ± SEM. *n= 5.* **P<0.05,***P<0.01,****,P<0.001, extract-treated groups compared with the DAL Group.

Table 2: Effect of methanol extract of *Capparis sepiaria* on hematological parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>DAL</th>
<th>DAL + MEDP 200 mg/kg</th>
<th>DAL + MEDP 400 mg/kg</th>
<th>DAL + 5-FU 20 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (%)</td>
<td>14.52±0.46</td>
<td>6.7±1.22*</td>
<td>7.98±0.49*</td>
<td>10.54±0.69*</td>
<td>9.86±0.99*</td>
</tr>
<tr>
<td>RBC (x10^6/mm^3)</td>
<td>13.14±0.56</td>
<td>7.5±0.5*</td>
<td>8.4±0.5**</td>
<td>9.52±0.39</td>
<td>11.3±0.60</td>
</tr>
<tr>
<td>PCV (%)</td>
<td>29.7±4.13</td>
<td>43.26±3.61c</td>
<td>35.5±3.45d</td>
<td>24.98±1.32d</td>
<td>22.62±1.57c</td>
</tr>
<tr>
<td>WBC (x10^6/mm^3)</td>
<td>0.625±0.13</td>
<td>5.74±0.7*</td>
<td>2.48±0.23d</td>
<td>1.7±0.19*</td>
<td>1.51±0.17d</td>
</tr>
<tr>
<td>Neutrophils (%)</td>
<td>37.6±1.74</td>
<td>53.8±7.01b</td>
<td>52.1±1.88</td>
<td>40.6±0.74*</td>
<td>38.4±1.69b</td>
</tr>
<tr>
<td>Lymphocytes (%)</td>
<td>60.4±2.33</td>
<td>46.5±0.74a</td>
<td>39.6±1.28</td>
<td>46.2±1.06</td>
<td>45.2±2.43a</td>
</tr>
<tr>
<td>Eosinophils (%)</td>
<td>3.3±1.03</td>
<td>1.6±0.4</td>
<td>2.5±0.67</td>
<td>3.4±5.0</td>
<td>4.4±1.03</td>
</tr>
<tr>
<td>Monocytes (%)</td>
<td>1.8±0.37</td>
<td>0.2±0.2</td>
<td>0.2±0.2</td>
<td>0.2±0.2</td>
<td>0.8±0.37</td>
</tr>
</tbody>
</table>

Data are expressed as the mean ± SEM, *n=5.* **P<0.05,****,P<0.01,****,P<0.001, Control Vs DAL. **P<0.05,****,P<0.01,**,**P<0.001, DAL Vs extract treated groups.

Table 3: Effect of methanolic extract of *Capparis sepiaria* on biochemical parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>DAL</th>
<th>DAL + MEDP 200 mg/kg</th>
<th>DAL + MEDP 400 mg/kg</th>
<th>DAL + 5-FU 20 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGPT(U/L)</td>
<td>24.6±2.7</td>
<td>52.6±2.49a</td>
<td>37.4±7.9*</td>
<td>31.6±0.78*</td>
<td>31±0.70c</td>
</tr>
<tr>
<td>SGOT(U/L)</td>
<td>112.6±27.6</td>
<td>173.8±15.1b</td>
<td>158.8±3.1c</td>
<td>122.8±1.24c</td>
<td>83.4±1.86c</td>
</tr>
<tr>
<td>Albumin(gm %)</td>
<td>2.4±0.64</td>
<td>11.2±0.2b</td>
<td>3.4±0.32</td>
<td>2.5±0.17</td>
<td>2.24±0.128c</td>
</tr>
<tr>
<td>Total Protein (gms%)</td>
<td>5.18±0.64</td>
<td>2.7±0.31a</td>
<td>3.61±0.95*</td>
<td>4.72±0.84c</td>
<td>6.3±0.57b</td>
</tr>
</tbody>
</table>

Data are expressed as the mean of results in 5 mice ± SEM. **P<0.05 and **,**P<0.01,**,**P<0.001, Control Vs DAL. **P<0.05,**,**P<0.01,**,**P<0.001, DAL Vs normal control; **P<0.05 and **,**P<0.01,**,**P<0.001, extract treated Groups Vs DAL group.

Table 4: Effect of methanolic extract of *Capparis sepiaria* on antioxidant parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>DAL</th>
<th>DAL + MEDP 200 mg/kg</th>
<th>DAL + MEDP 400 mg/kg</th>
<th>DAL + 5-FU 20 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>LPO (ng of MDA/mg protein)</td>
<td>0.23±0.02</td>
<td>2.01±0.29*</td>
<td>0.87±0.06</td>
<td>1.51±0.15</td>
<td>1.73±0.15c</td>
</tr>
<tr>
<td>SOD (U/mg protein)</td>
<td>0.15±0.01</td>
<td>0.01±0.01*</td>
<td>0.05±0.004</td>
<td>0.08±0.01</td>
<td>0.12±0.01c</td>
</tr>
<tr>
<td>CAT (U/mg protein)</td>
<td>0.96±0.13</td>
<td>0.11±0.01*</td>
<td>0.34±0.02</td>
<td>0.63±0.07</td>
<td>0.73±0.07c</td>
</tr>
<tr>
<td>GSH (mg/g wet tissue)</td>
<td>0.73±0.15</td>
<td>0.31±0.08</td>
<td>0.45±0.17a</td>
<td>0.53±0.16</td>
<td>0.56±0.17c</td>
</tr>
<tr>
<td>GPx (U/mg protein)</td>
<td>0.028±0.003</td>
<td>0.0016±0.005a</td>
<td>0.005±0.003</td>
<td>0.018±0.001a</td>
<td>0.019±0.003a</td>
</tr>
<tr>
<td>GST (U/mg protein)</td>
<td>0.026±0.003</td>
<td>0.002±0.0006*</td>
<td>0.010±0.0005</td>
<td>0.015±0.004*</td>
<td>0.018±0.003*</td>
</tr>
</tbody>
</table>

Data are expressed as the mean ± SEM, **P<0.001, DAL Vs normal control,**,**P<0.05,**,**P<0.01,**,**P<0.001, extract treated groups Vs DAL group.

Table 5: Effect of *Capparis sepiaria* on solid tumor growth

<table>
<thead>
<tr>
<th>Parameters</th>
<th>15th day</th>
<th>20th day</th>
<th>25th day</th>
<th>30th day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solid tumor volume in ml</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DAL control</td>
<td>0.08±0.01</td>
<td>2.0±0.3</td>
<td>3.9±0.7</td>
<td>6.4±1.19</td>
</tr>
<tr>
<td>MEDP 400</td>
<td>0.20±0.007</td>
<td>0.15±0.16</td>
<td>0.08±0.09**</td>
<td>0.03±0.22***</td>
</tr>
</tbody>
</table>

Data are expressed as the mean of results in 4 mice ± SEM. **,***,**P<0.01,**,**P<0.001, MEDP 400 Vs DAL Group.
Table 1. The percentage of cell viability 10%, 25%, 30%, 42%, 54%, 70%, 85%, 92% respectively. The IC_{50} value was found to be 600 μg/ml.

**Effect of MECS on Mean Survival Time:** The effect of MECS on mean survival time were shown in Table 2. On oral treatment of MECS to the tumor induced DAL mice, the mean survival time of DAL control group was found to be 13.5±0.96, while it increased to 19.2±0.58 (MECS 200 mg/kg), 22.5±2.24 (MECS 400 mg/kg) respectively in MECS treated groups and whereas the standard drug 5-fluorouracil (20 mg/kg)-treated group had a mean survival time 25.6±2.06.

**Effect of MEDP on Tumor Growth:** The effect of MECS on tumor growth response were shown in Table 2, after treatment with MECS (200 and 400 mg/kg) significantly (P<0.01, P<0.001) reduced the tumor volume, viable tumor cell count and (P<0.05, P<0.01) tumor packed cell volume in a dose-dependent manner as compared to that of the DAL Control group. Furthermore, nonviable tumor cell count at different doses of MECS were significantly (P<0.01) increased in a dose-dependent manner.

**Effect of MECS on Solid Tumor Growth:** There was reduction in the tumor volume of mice treated with MECS 400 mg/kg from 15th day to 30th day. On 30th day tumor volume of DAL control animals was 6.4±1.13 ml, whereas for the extract-treated group it was found to be 0.03±0.22 ml as shown in Table 5.

**Effect of MECS on Antioxidant Activity:** As shown in Table 5, in the DAL group, the LPO level was increased and SOD, CAT, reduced GSH, GP, GST levels were decreased significantly (P<0.001) as compared to the normal control. After treatment with MECS at different doses (200 mg/kg, 400mg/kg and 5-FU significantly decreased the LPO and increased the SOD, CAT, reduced GSH, GP, GST levels.

**Effect of MECS on Normal Peritoneal Cells:** The average number of peritoneal exudate cells per normal mouse was found to be 4.9x10^3. MECS (400 mg/kg) single treatment enhanced peritoneal cells to 9.4x10^4 while two consecutive treatments enhanced the number to 13.57 x 10^6.

**Effect of MECS on Biochemical Parameters:** As shown in Table 4, SGOT, SGPT, albumin levels were increased significantly (P<0.01) and total protein levels were decreased (P<0.05) as when DAL control group compared to the normal control group. After treatment with MECSS at the dose of 200 mg/kg, 400mg/kg and 5 FU significantly decreased the elevated SGOT, SGPT, albumin to normal levels and increased total protein levels.

**DISCUSSION**

The present study was carried out to evaluate the antitumor effect of MECS in DAL-bearing mice. The MECS-treated animals at the doses of 200 and 400 mg/kg significantly inhibited the tumor volume, packed cell volume, tumor cell count and brought back the hematological parameters to more or less normal levels. In DAL-bearing mice, a regular rapid increase in ascites tumor volume was noted. Ascites fluid is the direct nutritional source for tumor cells and a rapid increase in ascites fluid with tumor growth would be a means to meet the nutritional requirement of tumor cells [27]. Treatment with MECS increased the percentage of trypan blue positive stained dead cells in tumor bearing mice. The reliable criteria for judging the value of any anticancer drug are the prolongation of the life span of animals [28]. The MECS decreased the ascites fluid volume, viable cell count and increased the percentage of life span. It may be concluded that MECS by decreasing the nutritional fluid volume and arresting the tumor growth, this could be the reason for the increase life span of DAL-bearing mice. Usually, in cancer chemotherapy the major problems that are being encountered are of myelosuppression and anemia [29, 30]. The anemia encountered in tumor bearing mice is mainly due to reduction in RBC or hemoglobin percentage and this may occur either due to iron deficiency or due to hemolytic or myelopathic conditions [31]. After the repeated treatment, MECS able to reverse
the changes in hematological parameters hemoglobin content, RBC and WBC counts near to normal levels. This indicates that MECS is showing protective action on the hemopoietic system.

The generation of free radicals in vivo is a constant phenomenon due either to physiological metabolism or pathological alterations. These generated free radicals are the main cause of lipid peroxidation which is an autocatalytic free radical chain propagating reaction, is known to be associated with pathological conditions of a cell [32]. The oxidation of proteins, lipids, nucleotides and carbohydrates causes chemical modification, leads to damage of above. Malondialdehyde is the end product of lipid peroxidation, was reported to be more in cancerous cells when compared to non cancerous cells [33]. Cells have developed enzymatic systems (antioxidant enzymes) like SOD, catalase and glutathione which convert oxidants into non-toxic molecules, thus protecting the organism from the deleterious effects of oxidative stress. Glutathione (a tripeptide), usually the most prevalent intracellular thiol, functions directly or indirectly in a variety of cellular processes. Reduced glutathione (GSH) plays an important role in defense mechanisms by acting as an antioxidant or by reacting with electrophiles [34] and toxic agents to form conjugates that are eliminated from the cell [35]. SOD, CAT and glutathione peroxides are involved in the clearance of superoxide and hydrogen peroxide \( \text{H}_2\text{O}_2 \). SOD catalyses the diminution of superoxide into \( \text{H}_2\text{O} \), which has to be eliminated by glutathione peroxidase and/ or Catalase [36]. The inhibition of SOD and CAT activities as a result of tumor growth was also reported [37]. Similar findings were observed in the present investigation with DAL-bearing mice. MECS significantly reduced the lipid peroxidation and increased the glutathione levels in the DAL bearing drug treated mice. As above stated like the decreased levels of SOD, Catalase and GPx levels were observed in the present study, after drug treatment with different doses the levels of these enzymes were significantly increased.

Natural antioxidants are playing a great role in free radical scavenging activity. Some triterpenoids and flavonoids are found to have promising anticancer and antioxidant activity [38].

MECS shows the presence of triterpenes and flavonoids which may act as anticancer and antioxidant principles in the diseased condition [39]. In our earlier studies, we found that MECS possess antidiabetic and antioxidant properties [40]. The free radical hypothesis supported the fact that the antioxidants effectively inhibit the tumor and the observed properties may be attributed to the antioxidant and antitumor principles present in the extract.

**CONCLUSION**

The present study demonstrates that MECS increased the life span of DAL-tumor bearing mice and decreased the lipid peroxidation and thereby augmented the endogenous antioxidant enzymes in the liver. The above parameters are responsible for the antitumor and antioxidant activities of *Capparis sepiaria*.

**REFERENCES**


