Ameliorative Effect of Saffron Extract on Mice Bearing Solid Tumors

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Abstract

The present work aims to study the role of saffron in Ehrlich Ascites Carcinoma (EAC) in mice. Once the tumors were formed, the mice were divided into four groups (control, tumor, saffron, and saffron & tumor). Each group contained eight mice. At the end of experimentation, the mice were dissected and a histological examination of both liver and kidney was performed on all groups. Also, the levels of alanine transaminase (ALT), aspartate transaminase (AST), urea, creatinine, malonyl dialdehyde (MDA), superoxide dismutase (SOD), and catalase (CAT) were measured in all tested groups. Saffron extract improved the histological structures of both liver and kidney bringing them close to normal structures. They also reduced the elevated values of ALT, AST, Urea, Creatinine, and MDA towards normal values in significant and non-significant changes, increased the reduced levels of SOD and CAT to near normal values and significantly reduced tumor volumes. Finally, saffron modulated the destructed genomic DNA to be in normal patterns.

Keywords: Antioxidant, DNA Pattern, Ehrlich Ascites Carcinoma, Kidney, Liver, Mice, Saffron.

1. Introduction

Cancer, The most awful disease found among people, is a class of diseases designated by uncontrolled cell growth. More than 100 different types of cancer exist, and each is categorized by the type of cell initially affected. In many countries, the second most common cause of death after cardiovascular diseases is cancer (Jemal et al., 2007).[1] EAC is mentioned as an undifferentiated carcinoma and is originally hyperdiploid, with high transplantable ability, no-regression, quick propagation, shorter life span and 100% maliciousness (Kaleoglu and Isli, 1977). [2] EAC is used as ascites or a solid form according to the purpose. If ascites fluid has the tumor cell, the ascites form is acquired by intraperitoneal injection.


while the solid form is obtained through subcutaneous injection (Okay, 1998; Zeybek, 1996).^{[3,4]}

To treat cancer, different therapies are available. Chemotherapy and radiotherapy are the most common and have the best outlook, but they have many toxic side effects and induce the inhibition of the immune system (Diwanay et al., 2004).^{[5]}

Discoveries of alternative therapies which are natural, especially from plants, are used to defeat different forms of cancer with low toxic effects (Sakthivel and Guruvayoorappan, 2013).^{[6]}

A perfect anticancer agent must be cell-specific; it should kill the cancer cells without causing any damage to normal cells. Thus, natural products have now been considered effective anticancer drugs with the lowest host cell toxicity.

Saffron, *Crocus sativus*, is identified as Zaa’fran and used as an essential spice agent in making Arabic coffee. It was reported that saffron has a cytotoxic effect against Ehrlich ascites carcinoma solid tumors in mice and increases the lifespan of tumor bearing mice (Nair et al., 1991, 1992).^{[7,8]}

Saffron is identified with numerous chemical ingredients including crocin-1, picrocrocin, startry, vitamins, Bl and B2, fixed oils, carotenoids, colichicine, quercitin, proteins, wax and mucilage (Tarantilis et al., 1995).^{[9]}

Saffron and its chief carotenoid components may have the ability to inhibit and to cure different forms of cancer. Milad et al., (2011) revealed that the aqueous and ethanolic extracts of saffron displayed hepatoprotective effects against liver injuries stimulated by carbon tetrachloride (CCl4) in mice and significantly reduced the levels of AST and ALT in plasma. In vivo and in vitro experimentation proved that the active ingredients of saffron suppress cancer cell development and tumor induction. The anti-cancer features of saffron and its ingredients, such as safranal and crocin have been studied (Chryssanthi et al., 2007).^{[10]}

The anticancer effect of saffron is correlated with its antioxidative effect (Papandreu et al., 2011).^{[11]}

The imbalance between the antioxidants’ reaction ability and reactive oxygen species (ROS), leads to an oxidative stress, which induces different diseases such as cancer (Aghvami et al., 2006).^{[12]}

Russo et al., (2000)^{[13]}

mentioned that antioxidant defenses protect against free radicals. High levels of oxidative species (ROS) can induce damage to lipids, proteins and DNA. The antioxidants are either enzymatic or non-enzymatic. Enzymatic antioxidants are produced by the organism as catalase (CAT) and superoxide dismutate (SOD). The enzyme catalase acts as a defense system against H2O2, but the SOD enzyme acts on a superoxide (Mahadik and Scheffer, 1996).^{[14]}

Free radical-facilitated injuries may play a vital role in the stimulation of cancer. To study the importance of free radicals in the cancer

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^{[6]} Sakthivel K.M. and C. Guruvayoorappan. 2013. Acacia ferruginea effects (Sakthivel and Guruvayoorappan, 2013). A

therapies which are natural, especially from plants, are

used to defeat different forms of cancer with low toxic
effects (Sakthivel and Guruvayoorappan, 2013).^{[6]}


process, malonyl dialdehyde (MDA) levels, superoxide dismutase (SOD), and catalase (CAT) activities were determined in normal mice and mice bearing solid tumors treated or not treated with saffron. Asdaq and Inamdar (2010)\textsuperscript{[15]} mentioned that saffron induced a decrease in the elevated levels of AST, ALT and MDA in serum and in increasing the diminished levels of SOD and CAT.

This study aims to evaluate the antitumor activity of saffron extract \textit{in vivo} and \textit{in vitro} against mice bearing solid tumors induced with a subcutaneous injection of EAC cells.

\section*{2. Materials and Methods:}

\subsection*{Experimental Animals and Protocol}

Because Ehrlich Ascites Carcinoma (EAC) cells were stated to display greater initial growth and total cell count in female rather than male mice (Vincent and Nicholls, 1967)\textsuperscript{[16]} female mice were used in this study. Thirty two Swiss albino female mice (20-25 g in weight) obtained from the Animal House of the National cancer Institute, Cairo, Egypt, were used in the present study. The animals were randomized and housed under ambient room-temperature and relative humidity conditions. A commercial diet and water were provided ad libitum. The experiments were approved by the state authorities and followed Egyptian animal protection laws, as well as specific local institutional laws for animal protection under the supervision of authorized investigators.

The mice were divided into four groups, each containing eight mice. The mice of the 1\textsuperscript{st} group were served as a control group. The 2\textsuperscript{nd} group mice were injected subcutaneously with 0.2 ml of Ehrlich ascites carcinoma (EAC) which contains 3 × 10\textsuperscript{6} cells. The 3\textsuperscript{rd} group mice were treated orally with the saffron extract at a dose of 100 mg/ kg body weight, three times weekly for a month. For the 4\textsuperscript{th} group, the mice were inoculated with (EAC) as in group 2 then treated orally with 0.1 ml saffron extract after 10 days of inoculation at a dose of 100 mg/ kg body weight three times weekly for a month.

\subsection*{Saffron Extract Preparation}

Saffron (\textit{Crocus sativus}) was purchased from local markets in Cairo, Egypt. A dried powder (10 g) from saffron was mixed with 100 ml of organic solvent (ethanol, hexane and ethyl acetate). The mixture was placed at room temperature for 24 h on a shaker at 150 rpm. The solution was filtered through muslin cloth and then re-filtered by passing it through a Whatman Filter No. 1. The filtrate thus obtained was concentrated by complete evaporation of solvent at room temperature to yield the pure extract. The stock solution of crude saffron extract organic solvent was prepared by mixing the appropriate amount of dried extract with the respective solvent to obtain a final concentration of 100 mg/ml. The solution was stored at 4°C after its collection in sterilized bottles until further use.

\subsection*{Induction of Ehrlich Solid Tumor and Determination of Tumor Volume}

A line of EAC cells was obtained from the Cancer Biology Department of the National Cancer Institute (Cairo, Egypt), and preserved by weekly intra-peritoneal transplantation of 3x10\textsuperscript{6} cells/mouse. Ehrlich ascites carcinoma (EAC) cells were collected from donor mice (Swiss albino) with 20-25 g in body weight and suspended in a sterile isotonic saline. A fixed number of viable cells (usually 3 × 10\textsuperscript{6} cells/20 g body weight) were injected subcutaneously to the right hind limb of the mice (Gothoskar & Ranadive, 1971).\textsuperscript{[17]} The tumor developed and became palpable in all injected animals 10 days after tumor inoculation.


The change in tumor volume (TV/mm³) was measured individually twice a week for one month starting from the 15th day using a Vernier caliper and calculated by the following formula: Tumor volume (mm³) = 0.52 × (minor axis) × (major axis)² (Noaman et al., 2008).

**In vitro study**

The cytotoxicity assay of saffron extract on Ehrlich ascites tumor cells and the cell viability test were measured microscopically by calculating the viability of tumor cells. The optimal concentration of saffron extract was estimated (at 100 mg/kg body weight). The viability percentage of tumor cells was measured after incubation with the saffron extract. According to El-Merzabani et al. (1979),[18] with some required modifications, the viability percentage of tumor cells was measured after incubation with the examined extract (saffron). The cell suspension was mixed with an equal volume of trypan blue (4 mg/ml) at the ratio 1:1 and incubated for 5 min at 37°C. The estimation of the total number of viable cells was done using a hemocytometer chamber (Hashim et al., 2014).[19] The percentage of viable cells was calculated by the formula:

\[
\text{Percentage viable cells} = [1.00 - (\text{Number of trypan blue stained cells / Total cells})] \times 100.
\]

The viability of the cells was 99% as judged by trypan blue exclusion assay.

**Biochemical analysis**

For enzyme determination, blood samples were collected from the animals after 4 weeks of treatment. Sera were obtained by centrifugation of the blood sample and stored at -20°C until assayed for biochemical parameters. Both alanine aminotransferase and aspartate aminotransferase (ALT and AST), liver functions and plasma urea and creatinine (kidney functions) were determined colorimetrically using test reagent kits (Mediserve Company; Egypt, for liver enzymes and Randox, UK, for kidney functions), according to the manufacturer’s instructions.

According to (Draper and Hadley, 1990)[20] the levels

<table>
<thead>
<tr>
<th>Groups</th>
<th>Tumor Volume (mm³) Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Untreated tumor</td>
<td>2.37 ± 0.1949</td>
</tr>
<tr>
<td>Tumor treated with saffron</td>
<td>1.386 ± 0.11****</td>
</tr>
</tbody>
</table>


of lipid peroxidation product MDA (malondialdehyde) was estimated using the thiobarbituric acid (TBA) assay based on the release of color complex due to TBA’s reaction with MDA. Catalase (CAT) activity was defined by the assay based on the rate of hydrogen peroxide/ammonium molybdate complex formation (Gonenc et al., 2006).\[21] The activity of superoxide dismutase (SOD) was determined according to the method of Woolliams et al (1983)\[22] which is based on the inhibition of nitroblue tetrazolium (NBT) reduction by the xanthine - xanthine oxidase system as a superoxide generator.

**DNA fragmentation assay**

DNA fragmentation testing by agarose gel electrophoresis in all tested groups was determined by the method described by Tayeb and William (1999).\[23] The total genomic DNA was isolated from mice liver and kidney tumors belonging to different groups by using a DNA extraction kit (TIANamp Genomic DNA Kit) and analyzed by electrophoresis on 1.5% agarose gel containing 0.1 mg/ml ethidium bromide and visualized under an UV illuminator.

**Histopathological examination**

The treated animals and their controls were killed by cervical dislocation and quickly dissected. The liver and kidney were removed and fixed in Bouin’s fluid. After 24 hours, the tissues were rinsed three times in 70% ethanol, dehydrated using a graded ethanol series and then embedded in paraffin wax. Paraffin sections were cut into 5 micrometers thick slices and stained with haematoxylin and eosin for light microscope examination. The sections were viewed and photographed (Banchroft et al., 1996).\[24]

**Statistical analysis**

The results were expressed as mean ± SD of different groups. The differences between mean values were evaluated by one way analysis of variance ANOVA followed by Tukey-Kramer multiple comparison test (Armitage and Berry, 1987)\[25] using Graph Pad Prism software. P values < 0.05 were considered to be statistically significant.

### 3. Results:

#### Tumor size:

Measurements of the tumor in mice EAC-bearing tumor and saffron-tumor mice showed that the saffron extract reduced the tumor volume in a very extremely significant way (p < 0.0001) (Table 1).

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In vitro antitumor activity of saffron on EAC:

The Ehrlich ascites carcinoma cells appear bright (not colored) and intact in Figure 1 (A). The viability of EAC was very high (Tumor-Untreated). On the other hand, in Figure 1 (B), Ehrlich ascites carcinoma cells treated with saffron appear to be colored with trypan blue. Animals bearing EAC cells treated with saffron showed a significant decrease in the total viable EAC cell count in comparison to non-treated tumor bearing mice.

Biochemical results:

**Effect of saffron extract on kidney functions**

Data in Table (2) showed that the values of urea recorded an extremely significant elevation (P ≤ 0.001) in the sera of the tumor group mice compared to the control group. The mice treated with saffron showed non-significant values of urea compared to control (P > 0.05). On the other hand, the values of urea in mice – bearing solid tumors and treated with saffron were reduced from extremely significant (P ≤ 0.001) to very significant (P ≤ 0.01). Data in Table (2) shows that the values of creatinine recorded a very significant elevation (P ≤ 0.01) in the sera of the tumor group mice compared to the control group. In relation to mice treated with saffron, the recorded values of creatinine exhibited a non-significant change (P > 0.05) in relation to control values. On the other hand, the recorded values of creatinine in mice – bearing solid tumors treated with saffron still recorded extremely significant (P ≤ 0.001) to very significant (P ≤ 0.01).

### Table 4. Effect of saffron extract on MDA, SOD and CAT activities in different mice groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>MDA (nmol/g)</th>
<th>SOD (U/g)</th>
<th>CAT (U/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>4.038±0.00557</td>
<td>62.57±0.5831</td>
<td>29.00±1.000</td>
</tr>
<tr>
<td>Tumor</td>
<td>10.96±0.277***</td>
<td>30.64±1.704***</td>
<td>12.33±1.528***</td>
</tr>
<tr>
<td>Saffron</td>
<td>4.215±0.1050</td>
<td>60.17±0.5114**</td>
<td>27.33±1.528$</td>
</tr>
<tr>
<td>Saffron + Tumor</td>
<td>4.541±0.1095**</td>
<td>57.63±1.487**</td>
<td>21.67±1.528**</td>
</tr>
</tbody>
</table>

All data are expressed as mean ± SD.

(****) very extremely significant    P ≤ 0.0001

(*** ) extremely significant            P ≤ 0.001

( ** ) very significant                    P ≤ 0.01

(*) significant                           P ≤ 0.05

($) not-significant                      P > 0.05

**Figure 2.** Gel electrophoresis of tumor genomic DNA (A), liver genomic DNA (B) and kidney genomic DNA (C) in different animal groups. Lane 1: DNA ladder, Lane 2: Control, Lane 3: Tumor, Lane 4: Saffron and Lane 5: Saffron + Tumor.

**Figure 3.** Photomicrograph of histological structure of the kidney of a control mouse showing normal glomeruli (G) and normal renal tubules (RT). H&E, X400
a very significant elevation (P ≤ 0.01) in relation to the control group.

Effect of saffron extract on liver functions

Data in *Table (3)* showed that the values of Alanine Transaminase (ALT) estimated in the mice’s blood sera exhibited elevated values in the tumor group compared with the control group (P ≤ 0.0001). The mice treated with saffron showed a moderate elevation in the values of ALT to record a very significant value (P ≤ 0.01) in relation to the control group. On the other hand, the recorded values of ALT were still very extremely significant (P ≤ 0.0001) in tumor groups treated with saffron when compared with the control. It was obvious that the recorded values were diminished.

Data in *Table (3)* showed that the values of aspartate transaminase (AST) were also estimated in the mice blood sera and showed an elevation in the tumor group compared with the control group (P ≤ 0.0001). The mice treated with saffron showed a slight increase in AST values to record only a significant elevation (P ≤ 0.05) in relation to control values. On the other hand, the recorded AST values in tumor groups treated with saffron decreased from very extremely significant high (P ≤ 0.0001) to record an extremely significant elevation (P ≤ 0.001) when compared with the control values.
**Effect of saffron extract on oxidative and antioxidant enzymes**

The recorded data in Table 4 revealed that MDA values recorded a very significant elevation (P ≤ 0.0001) in the sera of mice bearing solid tumors compared to the control group. Mice treated with saffron showed nearly the same values of MDA levels as found in the control group and showed a non-significant change (P > 0.05) compared to normal values. Saffron induced inhibition in MDA levels in tumor groups from a very extremely significant change (P ≤ 0.0001) to record only a very significant elevation (P ≤ 0.01) when compared to the control group.

The recorded data in Table 4 revealed that the SOD and CAT values in mice bearing solid tumor recorded a very extremely significant (P ≤ 0.0001) decrease when compared to the control group. Mice treated with saffron showed a very significant reduction in SOD values and nearly normal CAT values (P > 0.05) when compared to control values, respectively. On the other hand, the recorded values of both SOD and CAT were elevated from very extremely significant (P ≤ 0.0001) to a very significant change (P ≤ 0.01) in the tumor group treated with saffron when compared to the control group.

**DNA Fragmentation:**

DNA isolated from the tumor, liver and kidney tissues of mice treated with EAC showed a complete degra-
Figure 12. Photomicrograph of liver’s histological structure in a mouse bearing solid a tumor treated with saffron showing some ameliorations in the hepatic structure. Blood sinusoids (BS), central vein (CV), hepatic cells (HC), Kupffer cells (KC) and fatty degeneration (FD). H&E, X400.

Different histopathological effects of EAC cells on the renal structure were also observed in Figure 5. Glomerular atrophy, the glomerular sub-capsular space appeared absent or very narrow, the renal tubules were degenerated and interstitial edema was also detected.

Mice which received saffron extract showed that that there are no pathological effects on the renal tissue and the kidney’s histological structure appeared normal and without any harmful effects. The kidney cortex of a normal mouse after saffron extract treatment showed normal renal tubules (RT) and glomeruli (G) (Figure 6).

In mice bearing solid tumors treated with saffron, there was a marked improvement of the histological structure of the kidney. This is obviously observed in Figure 7.

Liver:

The control mice showed the normal structure of the liver. The liver was formed from polygonal lobules. The outlines of the lobules were indistinct. The hepatocytes were polyhedral in shape, had vesicular spherical nuclei with prominent nucleoli and eosinophilic cytoplasm. The hepatocytes were arranged in cords that radiated out from the center of each lobule where the central vein is situated. Between these hepatic cords were the hepatic sinusoids, the hepatic sinusoids are localized between the cords and contained a fine arrangement of Kupffer cells (Figure 8).

Enormous histopathological alterations were observed in the liver of mice bearing solid tumors, an enlarged and congested central vein, numerous focal lesions of infiltration of tumor cells mixed with leukocytes. Signs of tumor metastasis in the liver tissue were also obvious, the absence of blood sinusoids and the Kupffer cells were more abundant than usual (Figure 9). The fatty degeneration of hepatic tissue is noticeable in Figure 10.

Liver sections obtained from mice treated with saffron extract are showing a normal liver structure without any harmful effects (Figure 11). While the hepatic structure of the mice bearing solid tumors and treated with saffron extracts revealed some improvements, the fatty degeneration and congested and enlarged central vein were as still found (Figure 12).
4. Discussion:

The present investigation was carried out to evaluate the antitumor activity and antioxidant status of saffron extract in EAC tumor bearing mice. Ascites fluid is the direct nutritional source of tumor cells. A rapid increase in the ascites fluid with tumor growth would be a means to meet the nutritional requirements of tumor cells (Rajeshwar et al., 2005).[26] This hypothesis was evident in the present study since the inoculation of EAC cells into the mice caused a significant increase in the tumor volume as found in Table 1. The treatment with saffron extract significantly decreased tumor growth as mentioned in Table 1, in agreement with Vijaya, (2011).[27]

Synthetic anticancer drugs cause the nonspecific killing of cells, whereas natural products offer protective and therapeutic actions to all cells with low toxicity (Reddy et al., 2003).[28] Thus, saffron was chosen as an anticancer natural product in this study.

The anti-tumor activity of saffron extract on EAC in vitro leads to a powerful cytotoxic effect, in concomitance with Amnish who reported that the oral administration (200mg/kg body wt.) of saffron extract leads to potential cytotoxic effects on EAC in vitro.

EAC inoculation in mice significantly increased the levels of serum aspartate transaminase (AST) and serum alanine transaminase (ALT). The results of the present study revealed that EAC induced hepatotoxicity in treated mice. These hepatotoxic effects are characterized by many histopathological alterations and elevation of ALT and AST serum levels. The same finding was approved by Abou Zaid, A.R.O, Hassanein, M.R.R., El-Senosi, Y.A.M and F. El-Shiekha. 2011. Ameliorative effect of curcumin and tannic acid on tumor-induced in female mice. Benha Veterinary Medical Journal, 1 61-69.

The recorded increase in plasma ALT and AST activities in tumor bearing mice of the present study might be due to the generalized destruction of liver cells and the release of AST into the plasma after tumor induction. The liver sections of the EAC-inoculated animals showed an enlarged and congested central vein, enlarged blood sinuoids, leucocytic infiltration and cytoplasmic vacuolar degeneration. This finding was in agreement with Bhattacharyya et al. (2007)[30] and Chakraborty et al. (2007).[31] Saffron extract showed a significant effect on hepatic injury induced by CCl4, caused the reduction in ALT and AST hepatic enzymes and ameliorated the histological disorders inducted in the liver. This finding confirmed the result of this study correlated with the role of saffron in decreasing the hepatotoxic effects of EAC tumor cells.

Serum urea and creatinine level elevation in clinical experiments means renal dysfunction, so the measured serum urea and creatinine levels determine the amount of kidney damage. A very highly significant increase in tumor-bearing female mice in serum urea concentration was confirmed by the results observed by Abou Zaid et al., (2011)[29] and Hussein and Azab (1997)[32] who found a highly significant increase in the plasma urea concentration in tumor-bearing mice. Such increase in blood urea concentration was attributed to the tumor’s catabolic effect and the increase in urea production. A very significant increase in serum creatinine concentration in tumor bearing mice was also reported, and this finding is in concomitance with those reported by Hussein (2003).[33] Results showed

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that saffron extract administration leads to nearly normal renal structure and normal hepatic structure as found in control kidney and liver. This finding agrees with Bahmani et al. (2014) who reported that the histopathological examination of the kidney and liver tissue sections of new born mice in the experimental group, of which the mothers received different doses of saffron, did not show any structural and pathological changes.

Saffron also exhibits anti-cancer effects in other types of animal cancer, which may be attributed to its antioxidant and pro-apoptotic actions on cancer cells. Oral administration of saffron is more effective, which may be attributed to its B-carotene precursor properties. Saffron also induces antioxidant enzymes and reduces the toxic effects of cancer drugs. Saffron and its constituents have cancer preventive effects and selective toxicity against cancer cells without having any toxic effects on normal cells.

Serum superoxide dismutase (SOD) and serum catalase (CAT) showed a very significant decrease in the Ehrlich group (Abd El-Aziz et al., 2014). It was also mentioned that serum malondialdehyde (MDA) showed a significant increase in the Ehrlich group. This finding is in concomitance with our results.

MDA is an important oxidative metabolite of polyunsaturated fatty acids consisting of biomembrane. MDA is often seen as an indicator of the oxidation status in cells or tissues. Thus, a high level of MDA is detrimental to cells and tissues and leads to a loss of their normal biofunction (Cheng et al., 2011). It was reported in this study that saffron extract has the ability to modulate the activities of antioxidant enzymes by increasing the levels of superoxide dismutase and catalase and reducing the level of malondialdehyde. This finding was confirmed by Hossein and Hamid (2005).

The mice subcutaneously inoculated with Ehrlich ascites cells showed a marked DNA fragmentation. The ethanolic extract of Crocus sativus (Saffron) had an inhibitory effect on DNA and RNA synthesis in isolated nuclei and suppressed the activity of purified RNA polymerase II. It was also reported that saffron extract reduced the growth rate of cancer cells by inhibiting nucleic acid synthesis and enhancing the anti-oxidative system, inducing apoptosis (Gutheil et al., 2011). These findings were in accordance with the results of this work.

**Conclusion:**
Ehrlich ascites carcinoma (EAC) has extremely harmful effects on all parameters investigated in this study. EAC significantly increased in the tumor volume the levels of liver function enzymes (ALT and AST), kidney function enzymes (urea & creatinine) and the oxidant enzyme Malondialdehyde (MDA). On the other hand, EAC considerably reduced the levels of antioxidant enzymes, superoxide dismutase (SOD) and catalase (CAT), and caused detrimental histopathological effects to the liver and kidneys. Finally, EAC induced DNA fragmentation. Saffron extract in mice-bearing solid tumors significantly modulated the levels of ALT, AST, urea, creatinine, MDA, SOD and CAT to be close to normal values. Saffron extract also induced recovery in the histological structures of both liver and kidney. It also restored the normal pattern of DNA. Saffron extract had no negative effects on the control group mice.

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