AMELIORATIVE EFFECT OF CURCUMIN AND TANNIC ACID ON TUMOR-INDUCED IN FEMALE MICE

Omayma A.R. Abou Zaid, Mohammed R.R. Hassanein, Yakout A. EL-Senosi, Mohammed F. EL-Shiekha

Department of Biochemistry, Faculty of Veterinary Medicine, Benha University, Egypt.

ABSTRACT

This study was carried out on 220 female mice, 12-14 weeks old and weighted 25-30 gm. Mice were classified into two main large experiments. Experiment 1: Non-tumor bearing mice (NTB) Included 100 of animals and divided into four groups each one comprised 25 mice. Group 1: NTB- control saline treated. Group 2: NTB-treated with curcumin orally (350 mg/kg/day) for 6 weeks. Group 3: NTB-treated with tannic acid orally (160 mg/kg/day) for 6 weeks. Group 4: NTB-treated with curcumin and tannic acid orally at ratio (50%:50%) for 6 weeks. Experiment 2: Tumor bearing (TB) mice. Included 120 of animals and divided into four groups each one comprised 30 mice. Group 1: TBM-control saline treated. Group 2: TBM-treated with curcumin orally (350 mg/kg/day) for 6 weeks. Group 3: TBM-treated with tannic acid orally (160 mg/kg/day) for 6 weeks. Group 4: TBM-treated with curcumin and tannic acid orally at ratio (50%:50%) for 6 weeks. Blood samples were collected from all animals groups after 2, 4 and 6 weeks from treatment. Serum were separated and processed directly for (AST and ALT) activities, (urea, creatinine, L-MDA) concentration and catalase activity determination. The obtained results revealed that, a very highly significant increase in serum AST, ALT, urea, creatinine and L-MDA concentration. On contrary, a highly significant decrease in serum catalase activity was observed in tumor bearing mice when compared with control. The results of this study indicated that curcumin and/or tannic acid treatment has potential benefits in cancer treatment.

KEY WORDS: Chemoprotective, Curcumin, Tannic acid, Tumor

1. INTRODUCTION

Cancer is a hyper proliferative disorder marked by metastasis into the vital organs of the body through invasion and angiogenesis. Cancer chemotherapy is often associated with the side effects on immune cells. Thus, the prerequisites for anti cancer drugs are to ensure no damaging effects on the immune cells, failing which the drug may completely terminate the subsided immune response in tumor-bearing host [1]. Curcumin, a polyphenolic compound extracted from rhizomes of Curcuma species, has been shown to possess anti inflammatory and antitumor properties [23]. Tannic acid (TA), a glucoside of gallic acid polymer which is found, along with other condensed tannins, in several beverages including red wine, beer, coffee, black tea, green tea, and many foodstuffs .It has been shown to possess anti-bacterial, anti-enzymatic and antitumor properties [3]. Curcumin may inhibit chemotherapy-induced apoptosis in animal models of
Omaya A. R. Abo Zaid et al. (2011) investigated the potential protective effect of curcumin and tannic acid treatment on experimentally induced tumors in female mice. They aimed to explore the role of these natural compounds in chemoprevention and further expanding their use in the field of cancer prevention.

2. Material and Methods

2.1. Animals

A total of 220 Australian female albino mice of 12-14 weeks old age and weighing 25-30 gm were used in the experimental investigation of this study. Mice were obtained from the Research Institutes of Ophthalmology, Giza, Egypt. Animals were housed in separate metal cages, fresh and clean drinking water was supplied ad-libitum through specific nipple. Mice were kept at a constant environmental and nutritional condition throughout the period of the experiment.

2.2. Tumor Induction:

The experimental induction of tumor in female mice was carried out at the National Cancer Institute Egypt. Every 1 ml of Ehrlich ascites adenocarcinoma was diluted with 4 ml of normal saline. Each mouse was injected subcutaneously (S/C) in the medial aspect of the right thigh with 0.2 ml of Ehrlich ascites adenocarcinoma (2.5 × 10⁶ tumor cells with single cell suspension) [30]. The tumor developed and became palpable in all injected animals at 5-7 days post tumor inoculation.

2.3. Experimental Design:

The experimental work was classified into two main large experiments as follow:

2.3.1. Experiment A: Non-tumor Bearing Mice. "NTB-Mice"

Included 100 of female mice divided into four groups, each one consisting of 25 animals placed in separate metal cages and classified as follows:

Group 1: Non tumor bearing control (NTB-C) administered with 0.2 ml of normal saline.
Group 2: Non tumor bearing (NTB-Cur) treated with curcumin orally administered daily at a dose level of (350 mg/kg/day) for 6 weeks.
Group 3: Non tumor bearing (NTB-Tan) treated with tannic acid orally administered daily at a dose level of (160 mg/kg/day) for 6 weeks.
Group 4: Non tumor bearing (NTB-Cur+Tan) treated with curcumin and tannic acid orally and daily at ratio of (50%:50%) for 6 weeks.

2.3.2. Experiment B: Tumor Bearing Mice. "TB-Mice"

A total number of 120 female TB-mice were divided into four groups, each one included 30 mice placed in separate metal cages and classified as follows:

Group 1: Tumor bearing control (TB-C) administered with 0.2 ml of normal saline.
Group 2: Tumor bearing (TB-Cur) treated with curcumin orally administered daily at a dose level of (350 mg/kg/day) for 6 weeks.
Group 3: Tumor bearing (TB-Tan) treated with tannic acid orally administered daily at a dose level of (160 mg/kg/day) for 6 weeks.
**Group 4**: Tumor bearing (TB-cur+tan) treated with curcumin and tannic acid orally and daily at ratio of (50%: 50%) for 6 weeks.

2.4. **Sampling**: Blood samples were collected in the morning after overnight fasting from all mice by decapitation every 2, 4, 6 weeks from the onset of treatment, then obtained in dry and clean tubes and serum was separated by centrifugation at 3000 rpm for 15 minutes. The clear serum were aspirated by Pasteur pipette and received in dry sterile sample tube, processed directly for enzymes determination, then kept in a deep freeze at -20°C until used for subsequent biochemical analysis.

2.5. **Biochemical analysis**: Serum (AST and ALT) activity, urea, creatinine, L-MDA, catalase were analyzed colorimetrically according to the methods described by Reitman and Frankel [19], Searcy et al. [22], Schirmeister et al. [21], Johansson and Borg [11], respectively.

2.6. **Statistical analysis**: The obtained results were statistically analyzed using student t-test and F-test according to Snedecor and Cochran [24].

3. **RESULTS AND DISCUSSION**

The presented data in table (1) revealed that, a very highly significant increase in serum (AST and ALT) activities, urea, creatinine and L-MDA concentration were observed in TB female mice. Meanwhile, a highly significant decrease in plasma catalase activity was observed in tumor-bearing female mice during the experimental period as compared with control. Similarly, Rafei et al. [18] recorded that, a rise in plasma bilirubin and hepatic enzyme activities were observed in tumor bearing rats is the results of changes in the liver indicated by the presence of tumor. The recorded increase in plasma ALT and AST activities in tumor bearing mice of the present study might be due to generalized destruction of liver cells and release of AST into plasma after tumor induction. On the other hand, a very highly significant increase in tumor-bearing female mice in serum urea concentration was confirmed by the results observed by Hussein and Azab [10] who observed that, there was a highly significant increase in plasma urea concentration in tumor-bearing mice. The author attributed such increase in blood urea concentration to catabolic effect of tumor and the increase in urea production.

Our results demonstrated a very highly significant increase in serum creatinine concentration in tumor bearing mice and this agree with those reported by Hussein [9] who observed a significant increase serum creatinine level in mice-bearing Ehrlich ascites carcinoma due to muscle necrosis. Also, the highly significant increase in serum L-MDA concentration in tumor bearing mice in the current work is congruent with the results reported by Hayat [7] demonstrated that, lipid peroxidation level was significantly increased in blood, liver and tumor tissues of (EAC) mice when compared with control group.

On the other hand, a very highly significant decrease in plasma catalase activity in tumor-bearing female mice is agreed with similar results reported by Bozzi et al. [2] that showed a very low catalase activities observed in tumor cells. Moreover, Marklund et al. [15] noticed that, Very large differences in catalase activity among the tissues and cell lines. Most neoplastic cell lines were low in catalase activity although some lines like the promyelocytic leukemia cell line HL 60 possessed high catalase activity.

The obtained results in table (2) revealed that, in TBM (cur) group showed a significant decrease in serum (AST) activity after 4 and 6 weeks as compared to control (S) group. Furthermore, a
significant increase after 2 weeks followed by a significant decrease after 4 and 6 weeks as compared to (tan) and (cur+ tan) treated groups. On the other hand, a significant decrease after 2 and 6 weeks as compared to control (S). Furthermore, a significant decrease observed all over the experimental period as compared to (tan) and (cur+ tan) treated groups. Similar results were reported by Yousef et al. [28] who showed that, curcumin decreased the induction of (AST and ALT) activity of rats treated with Sodium arsenite. The author attributed such decrease in transaminase enzymes to administration of curcumin preserved the structural integrity of the hepatocellular membrane. This was evident from the reduction in the enzyme activities against the arsenic induced rise in the enzyme levels in plasma. It could be suggested that the leakage of enzymes because of liver injury is prevented by the liver cell membrane stabilizing action of curcumin.

Administration of (tan) to TBM showed a significant decrease in serum (AST) activity after 2 weeks as compared to control (S) group. Furthermore, a significant decrease after 2 and 4 weeks as compared to (DMSO) group. Moreover, a significant decrease after 2 weeks followed by a significant increase after 4 and 6 weeks as compared to (cur) treated group. Also, a significant increase after 6 weeks as compared to (cur+ tan) treated group. On the other hand, a significant increase in serum (ALT) activity after 4 weeks as compared to control (S) group. Furthermore, a significant increase after 2 and 4 weeks as compared to (DMSO) group. Furthermore, a significant increase observed all over the experimental period as compared to (cur) treated group. Moreover, a significant increase after 4 and 6 weeks when compared to (cur+ tan) treated group. Similar results were reported by Tikoo et al. [25] who observed that, Treatment of tannic acid significantly reduced the increased plasma levels of (ALT) and (AST) levels to normal in Azido thymidine (AZT) treated mice, indicating its hepatoprotective effect.

Administration of (cur) to TBM showed a significant decrease in serum urea concentration was observed all over the experimental period as compared to control (S), (DMSO) and (tan) treated groups. Moreover, a significant decrease after 2 and 4 weeks while a significant increase after 6 weeks as compared to (cur+ tan) treated group. Similar results were reported by Tirkey et al. [26] showed in studies with cyclosporine that, treatment with curcumin was significantly decreased the level of urea and creatinine because of its role as potent antioxidant.

These suggestions was confirmed by Farombi and Ekor [5] who found that, the preventive effect of curcumin on the gentamicin-induced decrease in the activity of glutathione peroxidase (GSHPx) and CAT could contribute to the restoration of markers of renal tubular injury. It seems reasonable to assume that curcumin is able to suppress nephrotoxicity in kidney, as it was demonstrated in studies with adriamycin [27].

Our results in (TBM-tan) group showed a significant decrease in serum urea concentration was observed all over the experimental period as compared to control (S) group. Mean while, a significant increase all over the experimental period as compared to (cur) treated group. Moreover, a significant increase after 6 weeks when compared to (cur+ tan) treated group. Similar results were reported by Prasad et al. [17] who found that, there was significant reduction in the elevated levels of marker parameters of kidney toxicity, BUN and serum creatinine by treatment with Terminalia chebula extract due to presence of tannic acid. The author attributed this reduction to the highly antioxidant effect of tannic acid.

Administration of (cur) to TBM showed a significant decrease in serum creatinine concentration was observed all over the
Chemoprotective effect of curcumin and tannic acid

Table (1): Mean values of serum AST (U/ml), ALT (U/ml) activities, urea concentration (mg/dl), creatinine concentration (mg/dl), L-MDA concentration (nmol/ml) and catalase activity(nmol/ml) of experimentally induced tumor in female mice and their control.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>2 weeks</th>
<th>4 weeks</th>
<th>6 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NTB</td>
<td>TBM</td>
<td>NTB</td>
</tr>
<tr>
<td>S. AST (U/ml)</td>
<td>27.00±1.26</td>
<td>51.40***±2.02</td>
<td>17.20±1.20</td>
</tr>
<tr>
<td>S. ALT (U/ml)</td>
<td>37.80±1.71</td>
<td>40.40±2.20</td>
<td>38.80±2.55</td>
</tr>
<tr>
<td>S. Urea concentration (mg/dl)</td>
<td>26.14±0.31</td>
<td>48.66***±1.07</td>
<td>26.82±0.38</td>
</tr>
<tr>
<td>S. Creatinine concentration (mg/dl)</td>
<td>1.29±0.032</td>
<td>2.38***±0.021</td>
<td>1.56±0.046</td>
</tr>
<tr>
<td>S. L-MDA concentration (nmol/ml)</td>
<td>7.99±0.56</td>
<td>12.36***±0.65</td>
<td>0.74±0.45</td>
</tr>
<tr>
<td>S. Catalase activity (nmol/ml)</td>
<td>1.43±0.015</td>
<td>1.28±0.022</td>
<td>1.28±0.010</td>
</tr>
</tbody>
</table>

Data are presented as (mean ± S.E) & S.E. = standard error.
* = a significant after 4 weeks. p < 0.05
** = a highly significant after 2 weeks. p < 0.01
***=a a very highly significant after 2 weeks. p < 0.001

Table (2): Effect of curcumin, tannic acid alone or in combination on serum AST (U/ml), ALT (U/ml) activities, urea (mg/dl), creatinine (mg/dl), L-MDA concentrations and catalase activity (nmol/ml) in NTB and TBM.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>TBM C/(s)</th>
<th>TBM (DMSO)</th>
<th>TBM (cur)</th>
<th>TBM (tan)</th>
<th>TBM (cur+tan)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. AST (U/ml)</td>
<td>2</td>
<td>53.40±2.20</td>
<td>54.80±1.95</td>
<td>51.82±2.31</td>
<td>43.40±2.76</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>58.20±3.2</td>
<td>62.40±3.80</td>
<td>33.20±1.82</td>
<td>48.40±4.66</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>81.20±3.18</td>
<td>79.40±4.24</td>
<td>13.60±1.74</td>
<td>77.82±2.03</td>
</tr>
<tr>
<td>S. ALT (U/ml)</td>
<td>2</td>
<td>40.40±1.7</td>
<td>37.90±1.22</td>
<td>33.00±1.87</td>
<td>42.40±1.71</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>36.80±2</td>
<td>35.00±2.23</td>
<td>36.60±3.18</td>
<td>79.60±2.22</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>84.80±2.17</td>
<td>84.60±3.23</td>
<td>21.80±1.49</td>
<td>82.60±2.46</td>
</tr>
<tr>
<td>S. Urea concentration (mg/dl)</td>
<td>2</td>
<td>48.66±1.07</td>
<td>55.74±1.40</td>
<td>43.74±1.48</td>
<td>31.99±0.44</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>54.33±0.81</td>
<td>55.91±0.48</td>
<td>32.24±0.46</td>
<td>27.16±0.40</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>52.82±1.13</td>
<td>60.83±0.45</td>
<td>40.49±0.62</td>
<td>33.41±0.59</td>
</tr>
<tr>
<td>S. Creatinine concentration (mg/dl)</td>
<td>2</td>
<td>2.38±0.021</td>
<td>2.44±0.019</td>
<td>1.23±0.037</td>
<td>2.27±0.017</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>3.24±0.046</td>
<td>3.46±0.036</td>
<td>1.40±0.032</td>
<td>1.96±0.029</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>3.76±0.032</td>
<td>3.84±0.066</td>
<td>1.58±0.023</td>
<td>1.91±0.043</td>
</tr>
<tr>
<td>S. L-MDA concentration (nmol/ml)</td>
<td>2</td>
<td>12.36±0.6</td>
<td>12.88±0.69</td>
<td>9.09±0.45</td>
<td>11.19±0.10</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>17.69±0.8</td>
<td>18.09±0.63</td>
<td>12.23±0.8</td>
<td>13.13±0.69</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>23.55±1.18</td>
<td>24.85±0.48</td>
<td>13.52±0.60</td>
<td>18.09±0.63</td>
</tr>
<tr>
<td>S. Catalase activity (nmol/ml)</td>
<td>2</td>
<td>1.28±0.022</td>
<td>1.20±0.019</td>
<td>1.41±0.020</td>
<td>1.22±0.021</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>1.13±0.041</td>
<td>1.00±0.038</td>
<td>1.77±0.030</td>
<td>1.44±0.022</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>1.03±0.025</td>
<td>0.94±0.050</td>
<td>2.02±0.049</td>
<td>1.85±0.030</td>
</tr>
</tbody>
</table>

Mean values with different subr script letters in the same rows are significantly different at (p < 0.05).

Experimental period as compared to control (S), (DMSO) and (tan) treated groups. Furthermore, a significant decrease after 2 and 4 weeks followed by a significant increase after 6 weeks as compared to (cur+tan) treated group.
Similar results were reported by Mokhtar et al. [29] who showed that, treatment with curcumin alone caused a significant decrease creatinine level due to The renoprotective effect of curcumin via scavenging of ROS is well documented. Administration of (tan) to TBM showed a significant decrease in serum creatinine concentration was observed all over the experimental period as compared to control (S) and (DMSO) groups. Mean while, a significant increase all over the
experimental period as compared to (cur) and (cur+tan) treated groups. Similar results were reported by Wang and Hikokichi [29] who reported that, Tannins of herba ephedra could improve renal function in adenine-induced chronic renal failure in rats, that causing highly significant decreased blood urea nitrogen (BUN) by 37%, creatinine (Cr) 35%.

Administration of (cur) to TBM showed a significant decrease in serum L-Malondialdehyde concentration was observed all over the experimental period as compared to control (S) group. Furthermore, a significant decrease after 6 weeks as compared to (tan) treated group. Similar results were reported by Khopde et al. [12] who found that, Pretreatment of curcumin to β-irradiated hepatocytes resulted in decreased lipid peroxidation and improved antioxidant status preventing the damage to the hepatocytes. This may be due to the antioxidant sparing action of curcumin. The presence of π conjugation in curcumin makes it more hydrophobic. As a result curcumin get localized in the lipid bilayer membrane. Curcumin, being lipid soluble, reacts with the lipid peroxyl radicals and acts as a chain terminating antioxidant.

A significant decrease in serum L-MDA concentration was observed in TBM (tan) group after 4 and 6 weeks as compared to control (S) and (DMSO) groups. Furthermore, a significant increase after 6 weeks as compared to (cur) treated group. Moreover, a significant increase after 4 and 6 weeks as compared to (cur+tan) treated group. Similar results were reported by Hassan et al. [6] were found that, there was a significant decrease in lipid peroxides, nitric oxide levels and the activity of catalase in the aluminium chloride treated rats. However, tannic acid could play a prophylactic role in reducing the oxidative damage in the brain tissue of aluminium chloride exposed rats that induce cancer. Also, Lin et al. [14] reported that, tannic acid has been reported to quench lipid peroxidation, prevent DNA oxidative damage and scavenge hydroxyl radical.

Administration of (cur) to TBM showed a significant increase in plasma catalase activity was observed all over the experimental period as compared to control (S), (DMSO) and (tan) treated groups. Furthermore, a significant increase after 2 and 4 weeks followed by a significant decrease after 6 weeks as compared to (cur+tan) treated group. Similar results were reported by Nazam Ansari et al. [16] who found that, Curcumin (300 mg/kg) pretreatment for 20 days in isoproterenol treated rats significantly increased the levels of myocardial endogenous antioxidants (superoxide dismutase, catalase, and tissue glutathione) as compared to pathogenic control rats.

TBM (tan) group showed a significant increase in plasma catalase activity after 4 and 6 weeks as compared to control (S) and (DMSO) groups. Furthermore, a significant decrease was observed all over the experimental period as compared to (cur) treated group. Furthermore, a significant decrease after 6 weeks as compared to (cur+tan) treated group. Similar results were reported by (El-Sayed et al. [4] investigated the effect of tannic acid on some biochemical parameters in Swiss albino mice and reported that, The administration of 20 mg tannic acid/kg body weight three times a week every other day for three weeks, enhanced the endogenous antioxidant capacity of the cells by increasing the activities of antioxidant enzymes (SOD, CAT, GSH-R, GST), GSH content and serum Cu2+ and Zn2+ levels Compared to the lead acetate-exposed group.

4. CONCLUSION AND RECOMMENDATION

Curcumin has potent chemopreventive activity against a wide variety of tumors and has great potential in the prevention
and treatment of cancer, also prevent LDL oxidation.

In addition, tannic acid exerts chemopreventative activity against cancer due to its content of polyphenols which has antioxidant and free radicals scavenging activity and trapping of activated metabolites of carcinogen.

So we recommended by using curcumin in our food as prophylactic and preventive for many diseases. Also, drinking tannic acid after food by times to take it is benefit and alone.

5. REFERENCES


التأثير الوقائي للكوركوزم وحمض التانيك على السرطان المحدث في إناث الجواد

محمد فتحي الشيخ - يعقوب عبد الفتاح السنوسي - محمد رجائي رجب حسانين - أميمه أحمد رجب أبو زيد
قسم الكيمياء الحيوية والأكيمكية - كلية الطب البيطري - جامعة بنها

الملخص العربي

� Vertically aligned text

 telah Aجريت هذه الدراسة بهدف البحث عن أدوية طبيعية تمنع انقسام الخلايا السرطانية بدون آثار جانبية. قسمت حيوانات التجربة محل الدراسة (202 فأرًا من الإناث) إلى تجربتين: التجربة الأولى- فئران لا تحمل أي ورم وتحتوى على 100 فأر والتي قسمت إلى 4 مجموعات: المجموعة الأولى- وتتحوى على 25 فأر تم تجريعها بالمحول الملحي- المجموعة الثانية- وتتحوى على 25 فأر تم تجريعها بالكوركوزم (350 mg/kg/day) لمدة 6 أسابيع- المجموعة الثالثة- وتتحوى على 160 mg/kg/day لمدة 6 أسابيع- المجموعة الرابعة- وتتحوى على 25 فأر تم تجريعها بحمض التانيك (350 mg/kg/day) لمدة 6 أسابيع. يتم تجريعها بخلاط متماثل من حمض التانيك والكوركوزم لمدة 6 أسابيع- التحصيلة الثانية- وهي التي تم زراعة السرطان بها وتحتوى على 120 فأر والتي قسمت إلى 4 مجموعات أيضا: المجموعة الأولى- وتتحوى على 30 من الفئران الحاملة للورم والتي تم تجريعها بالمحلول الملحي وهي مجموعة ضابطة سرطان- المجموعة الثانية- وتتحوى على 30 من الفئران الحاملة للورم والتي تم تجريعها بالكوركوزم (350 mg/kg/day) لمدة 6 أسابيع- المجموعة الثالثة- وتتحوى على 30 من الفئران الحاملة للورم والتي تم تجريعها بحمض التانيك (350 mg/kg/day) لمدة 6 أسابيع- المجموعة الرابعة- وتتحوى على 30 من الفئران الحاملة للورم والتي تم تجريعها بخلاط متماثل من حمض التانيك والكوركوزم لمدة 6 أسابيع. تم تجميع عينات الدم بعد الذبح وفصلها وقياس كلا من إنزيمات الكبد (ALT, AST), اليوبريا، الكرياتينين، وبعض الإنزيمات المضادة للأكسدة مثل المالونالدهيد و الكاتالاز. وأظهر النتائج وجود زيادة معنوية في تركيز كلا من ALT، اليوبريا، الكرياتينين والمالونالدهيد ونقص معنوي في تركيز إنزيم الكاتالاز في الفئران الحاملة للورم السرطاني بالمقارنة بالمجموعة الضابطة. وحدث تغير في هذه النتائج إلى الأفضل بعد التجريع بالكوركوزم و حمض التانيك. لذا نوصي بتناول الكوركوزم والشاي لوجود نسبة عالية في محض التانيك حيث أنهما مضادان للسرطان.