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Research Article
Antitumoral Effect of Tomentosin from *Inula viscosa* Plant on Mice with Ehrlich Acid Tumor

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Abstract
Background and Objective: Spontaneous or transplantable tumor models are kinetically similar to human cancer types and play a role in understanding the biology of carcinogenesis and in the development of chemo-preventive and chemo-suppressive drugs. In this study, the effect of tomentosin isolated from the *Inula viscosa* plant against Ehrlich ascites tumor (EAT), was carried out. **Materials and Methods:** *Inula viscosa* (Asteraceae) was collected from the vicinity of Kilis 7 Aralık University, Kilis, Turkiye and tomentosin was isolated. In this study, 7 groups of 6 mice were used in each group. The EAT was taken from stock mice and counted in a Cedex XS cell counter (Roche) and administered intraperitoneally to tumor groups in 0.2 mL PBS (phosphate-buffered saline) once at the beginning of the study. Tomentosin was administered intraperitoneally to groups in 3 doses (25, 50 and 100 mg/kg). Average weight change, total oxidant capacity (TOS), total antioxidant capacity (TAS) and superoxide dismutase enzyme (SOD) activity were examined. The liver, small intestine, large intestine and stomach were taken from sacrificed animals and examined histopathologically. The findings were statistically evaluated using ANOVA followed by Dunnett's Multiple Comparisons test in SPSS 17, with significance set at $p<0.05$. **Results:** The weight changes, SOD and TAS results of mice showed that tomentosin at a dose of 100 mg/kg reduced the tumor. It was determined that tumors in groups where tomentosin was administered together with tumors were morphologically reduced and this reduction was directly proportional to the dose of tomentosin. In the group in which 100 mg/kg tomentosin dose and Ehrlich ascites tumor were administered together, histopathological examination of kidney, small intestine, large intestine and stomach tissues showed less tumor involvement compared to other doses. **Conclusion:** Weight, biochemical and histological evaluations supported each other that tomentosin is effective in reducing tumors and it is thought that this study will be useful for future studies.

Key words: *Inula viscosa*, tomentosin, Ehrlich acid tumor, superoxide dismutase, total antioxidant capacity, total oxidant capacity

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

In 2020, an estimated 19.3 million new cancer cases and approximately 10.0 million cancer deaths occurred worldwide[1]. Researchers are conducting various studies in many cancer models against this difficult disease. Spontaneous or transplantable tumor models are kinetically similar to human cancer types and play a role in understanding the biology of carcinogenesis and in the development of chemopreventive and chemosuppressive drugs[2]. The Ehrlich tumor model used in the study first arose as spontaneous breast cancer in a mouse in 1907 and is specific to mice. This tumor model, which has a very aggressive structure, can be easily transferred from one mouse to another and results in 100% mortality[2]. To obtain the solid form of the tumor model, the tumor must be administered subcutaneously to the mouse and to obtain the ascitic form, the tumor must be administered intraperitoneally[2]. After the EAT cell is placed in the abdominal cavity, it causes the formation of ascitic fluid, which progresses over time and causes a local inflammatory reaction[3,4]. Ascitic fluid provides a direct nutrient source for tumor cells and is necessary for tumor growth[5]. Since cancer drugs have very strong side effects, researchers have turned to herbal treatment methods[6,7]. In phytotherapy, *Inula viscosa* or locally known as Taioon, is a perennial herb belonging to the Asteraceae family. *Inula viscosa* is used therapeutically due to its anticancer, antiseptic, anti-inflammatory, antipyretic, antimicrobial and antiulcerogenic properties. Tomentosin is a sesquiterpene lactone found in *Inula viscosa* and has a wide range of biological activities, especially cytotoxicity and anti-inflammatory[8]. In this study, tomentosin (Fig. 1), one of the natural sesquiterpene lactones obtained from the *Inula viscosa* plant, with a molecular weight of 248.3175 g/mol and a chemical formula[9] of $C_{15}H_{20}O_3$, was used.

With *in vivo* studies, it is easier to detect the side effects of the active substance in the body. They are also more clinically relevant. This study aimed to investigate the effect of tomentosin obtained from *Inula viscosa* (Asteraceae) against the Ehrlich ascites tumor model in mice.

MATERIALS AND METHODS

The applications related to the study were carried out at Gaziantep University in Türkiye between 2022 and 2024.

Plant supply and obtaining pure substance: *Inula viscosa* (Asteraceae) was collected from the vicinity of Kilis 7 Aralik University Campus and dried at Gaziantep University Biology Department. Tomentosin was purified by the following method:

- Plant samples were first extracted with hexane 5 times to remove lipophilic substances
- Then extracted with ethanol 5 times
- After removing ethanol, crude extract was separated into fractions by silica gel column chromatography (70-230 mesh) using chloroform and chloroform-acetone (9:1) mobile phase systems
- Each fraction was checked by thin-layer chromatography and fractions containing tomentosin were determined
- Fractions containing tomentosin were combined among themselves and pure tomentosin was obtained by removing the solvent
- Chemical structure of the purified tomentosin molecule was confirmed by 1H-NMR and 13C-NMR methods

Tumor formation: The Ehrlich ascites tumor model was provided by the Department of Anatomy, Erciyes University Faculty of Medicine, Kayseri, Turkey. Tumor tissues were transferred to the Gaziantep University Experimental Animal Research Center (GAUNDAM) and kept in stock animals for use in experiments. At the beginning of the experiment, fluid containing EAT cells was taken from the peritoneal cavity of the stock mouse and administered to the mice with a syringe.

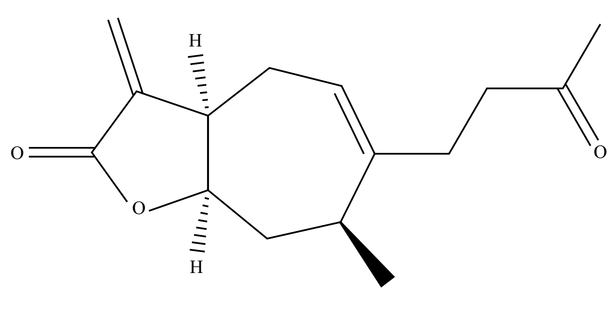

Fig. 1: Chemical structure of tomentosin[9]

Table 1: Details of substances administered, their respective doses and the number of animals used in each experimental group

Group	Duration of application	Number of animals in group
Group 1: 0.2 mL saline	15 days	6
Group 2: 1×10^6 EAT cells (1 time)+0.2 mL tween 80	15 days	6
Group 3: Tomentosin (100 mg/kg)	15 days	6
Group 4: 1×10^6 EAT cells (1 time)+5-fluorouracil (20 mg/kg)	15 days	6
Group 5: 1×10^6 EAT cells (1 time)+tomentosin (25 mg/kg)	15 days	6
Group 6: 1×10^6 EAT cells (1 time)+tomentosin (50 mg/kg)	15 days	6
Group 7: 1×10^6 EAT cells (1 time)+tomentosin (100 mg/kg)	15 days	6
Total number of animals to be used in the study		42

Supply of experimental animals and ethical approval: In this study, 42 male Balb-c mice (8-10 weeks old, 25-35 g) were used. The animals were taken from Erciyes University and assays were carried out in Gaziantep University Experimental Animal Research Center (GAUNDAM) after the quarantine period of 2 weeks.

Research application approval was obtained from the Gaziantep University Animal Experiments Local Ethics Committee for the study (Decision number: 2022/7-Protocol number: 238).

Formation of experimental groups: Power analysis software Power 3.9.1 was used to determine the number of animals used in the experiments. The groups of this study are shown in Table 1.

Tumor model creation: The fluid containing EAT cells was taken from the stock mouse with a syringe. They were counted in a Cedex XS cell counter (Roche Diagnostics, production location Germany) and administered intraperitoneally to each mouse at the beginning of the study, once in 0.2 mL of PBS (phosphate-buffered saline) containing 1×10^6 cells[10].

Active substance administration: In this study, tomentosin was used in 3 doses (25, 50 and 100 mg/kg)[11]. Tomentosin was administered intraperitoneally in 0.2 mL Tween 80 daily, 24 hrs after tumor inoculation. In the control groups, physiological serum and commercially available chemotherapeutic agent 5-fluorouracil (20 mg/kg) were administered intraperitoneally[11].

Determination of biochemical parameters: At the end of the study, cardiac blood was collected from all animals under ketamine (Ketalar, Parke Davis, Eczacıbaşı)-xylazine (Rotemar, Bioveta, Chech) (87.5/12.5 mg/kg to 0.1 mL/20 g b.wt.) anesthesia (IACUC Guidelines Anesthesia 2021) using a heparinized syringe. The serum of the blood samples was separated and total oxidant capacity[12] (TOS) (Rel Assay Diagnostics), total antioxidant capacity[13] (TAS) (Rel Assay Diagnostics) and superoxide dismutase (SOD) (Sigma-Aldrich/kit) enzyme activity were determined.

Histopathologic examination: At the end of the study, all animals were sacrificed and kidney, stomach, small intestine and large intestine tissues were removed and placed in 10% formaldehyde. After tissue tracing, sections were taken and stained with the "Hematoxylin-Eosin" method and preparations were prepared. The preparations were evaluated by light microscopy and the metastasis status of the tumor was determined.

Statistical analysis: At the end of the study, the statistical evaluation of the findings was performed according to the ANOVA+Dunnett Multiple Comparisons test method using the SPSS program 17 ($p<0.05$) was considered significant.

RESULTS

Weight: According to the weighing results from the beginning of the study, no change was observed in the weight of the animals in Group 1. In the tumor-applied groups, weight gain was observed in all groups except Group 4 due to tumor load and the highest weight gain was observed in Group 2, which was only applied EAT (Fig. 2). Among the groups that applied tumor and tomentosin together, the lowest weight gain was observed in Group 7, which was given a dose of 100 mg/kg. In Group 4, where EAT+5-fluorouracil was applied, a decrease in tumor load was observed due to the chemotherapeutic drug used, but it was observed that it caused side effects such as loss of appetite and malnutrition. Therefore, a decrease in the weight of the animals in this group was observed.

Biochemical parameters

Superoxide dismutase (SOD)/total protein: At the end of the experiment, the ratio of superoxide dismutase enzyme to total protein in blood tissue was analyzed. As can be seen in Table 2, SOD enzyme activity increased in the tumor group compared to the healthy group. This increase was found to be statistically insignificant according to an LSD test. However, a small difference was detected according to the Duncan test. In addition, SOD enzyme activity was found to be lower in 5-FU treated group compared to tomentosin treated groups. The SOD enzyme activity increased in tomentosin

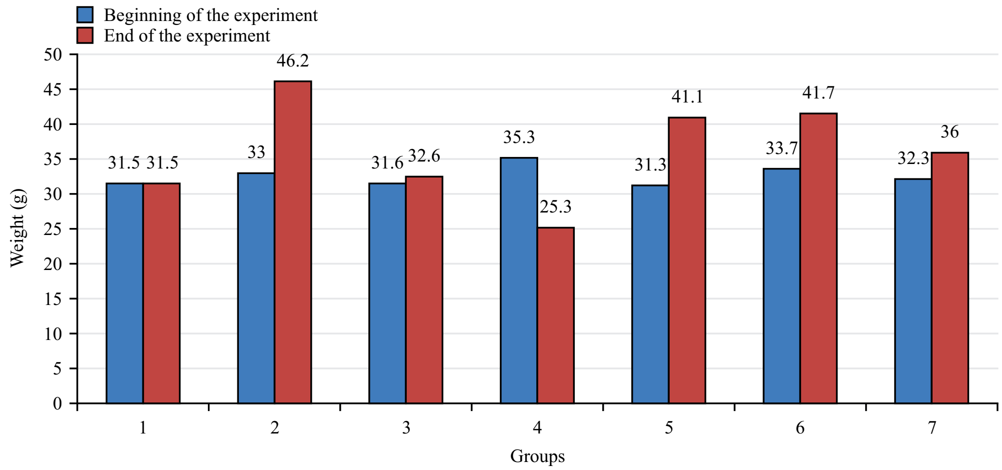

Fig. 2: Average weight of animals at the beginning and end of the experiment

Table 2: Superoxide dismutase (SOD) activity normalized to total protein content in different experimental groups

Group	Dose	Value
SF	0.2 mL	0.0013 ± 0.0001^{a}
EAT	1×10^{6}	0.0017 ± 0.0003^{ab}
Tomentosin	100 mg/kg	0.0015 ± 0.0003^{ab}
EAT+5-FU	20 mg/kg	0.0014 ± 0.0003^{a}
EAT+tomentosin	25 mg/kg	0.0018 ± 0.0006^{ab}
EAT+tomentosin	50 mg/kg	0.0019 ± 0.0003^{ab}
EAT+tomentosin	100 mg/kg	0.0021 ± 0.0009^{b}

While groups with the same letter indicate no difference, different letters indicate a difference between groups, EAT: Ehrlich ascites tumor, SF: Physiological serum and 5-FU: 5 fluorouracil

Table 3: Total antioxidant capacity (TAS) values measured across various experimental groups

Group	Dose	Value
SF	0.2 mL	1.01 ± 0.16^{b}
EAT	1×10^{6}	$0.60 \pm 0.16^{*a}$
Tomentosin	100 mg/kg	0.99 ± 0.13^{b}
EAT+5-FU	20 mg/kg	$1.30 \pm 0.13^{*bc}$
EAT+tomentosin	25 mg/kg	$1.13 \pm 0.23^{*bc}$
EAT+tomentosin	50 mg/kg	$1.26 \pm 0.44^{*bc}$
EAT+tomentosin	100 mg/kg	$1.43 \pm 0.12^{*c}$

While groups with the same letter indicate no difference, different letters indicate a difference between groups, EAT: Ehrlich ascites tumor, SF: Physiological serum and 5-FU: 5 fluorouracil

Table 4: Total oxidant capacity (TOS) in studied groups

Group	Dose	Value
SF	0.2 mL	13.40 ± 3.72^{b}
EAT	1×10^{6}	$9.06 \pm 1.97^{*a}$
Tomentosin	100 mg/kg	$8.88 \pm 2.17^{*a}$
EAT+5-FU	20 mg/kg	-
EAT+tomentosin	25 mg/kg	$12.77 \pm 3.53^{*ab}$
EAT+tomentosin	50 mg/kg	$20.79 \pm 4.24^{*c}$
EAT+tomentosin	100 mg/kg	$26.97 \pm 3.28^{*d}$

While groups with the same letter indicate no difference, different letters indicate a difference between groups, EAT: Ehrlich ascites tumor, SF: Physiological serum and 5-FU: 5 fluorouracil

treated groups. The greatest increase was observed in Group 7, which received 100 mg/kg tomentosin dose compared to healthy tissue. These results indicate that tomentosin increases SOD activity in tissues. However, these increases were not statistically significant according to the LSD test.

Total antioxidant capacity (TAS): When the group given only saline was compared with the tumor group, TAS capacity was significantly decreased in the tumor group compared to healthy tissue. When the other groups were compared with the tumor group, the TAS capacity in the group given tomentosin alone did not differ from the healthy tissue. On the other hand, both tomentosin administration and the positive control 5-FU increased TAS capacity. The present results show that tomentosin increased TAS capacity in tumor groups in a dose-dependent manner (Table 3).

Total oxidant capacity (TOS): The TOS values were lower in the tomentosin-only and EAT only groups compared to the healthy group. However, an increase was observed in the EAT+tomentosin (50 mg/kg) and EAT+tomentosin (100 mg/kg) groups compared to the healthy group (Table 4).

Histopathologic findings

Kidney: Kidney histology was preserved in both healthy kidneys and the group that received only tomentosin. Normal cortex, capsule and normal fat tissue around the capsule were observed (Fig. 3a and c). In Group 2, degeneration of the kidney capsule was observed and tumor involvement was observed, especially around the outer perimeter of the capsule (Fig. 3b). While kidney involvement was not observed in Group 4 animals that received EAT+5-FU, atrophy was observed in the subcapsular tubules (Fig. 3d). In Group 5 animals that received EAT+25 mg/kg tomentosin, the kidney capsule and subcapsular tubules had normal morphology, but tumor involvement was observed around the outer perimeter of the capsule (Fig. 3e). In Group 6 mice treated with EAT+50 mg/kg tomentosin, the kidney capsule and subcapsular tubules had normal morphology and tumor involvement was observed around the outer perimeter of the capsule (Fig. 3f). Normal morphology of the renal capsule and subcapsular tubules was observed in the kidney tissue of the 7th group of animals given EAT+100 mg/kg tomentosin. Tumor involvement continued around the outer periphery of the capsule, but tumor width was the lowest in the EAT+tomentosin groups (Fig. 3g).

Small intestine: When the results were evaluated, no tumor involvement was observed in the small intestine tissues of the 1st and 3rd group animals without EAT. The morphology of villus structure, submucosa, muscularis and serosa layers were found to be healthy only in the group given tomentosin (Fig. 4a and c). In the small intestines of the second group of animals in which the tumor was given alone, tumor involvement was observed in the submucosa and serosa layers. The integrity of the villus structures was preserved (Fig. 4b). No tumor was found in the small intestines of the 4th group mice treated with EAT+5-FU, but necrotic areas were observed in the crypts (Fig. 4d). In EAT+25 mg/kg tomentosin-treated Group 5 and EAT+50 mg/kg tomentosin-treated Group 6 animals, tumor tissue was observed in the muscularis and serosa layers of the small intestines and tumor cells were also present in the submucosa (Fig. 4e-f). In the small intestine tissues of EAT+100 mg/kg tomentosin-treated mice, tumor tissue was present only in the serosa layer and its size decreased compared to the other groups (Fig. 4g).

Large intestine: According to the data, the large intestines of Group 1 and 3 animals without tumors had a normal appearance. In the group that was given only tomentosin, the morphology of the crypt, submucosa, muscularis and serosa layers of the large intestine was found to be healthy (Fig. 5a, c). In group 2 animals, tumors were seen only in the serosa layer (Fig. 5b). In group 4 (EAT+5-FU), no tumor involvement was observed in the large intestine tissues (Fig. 5d). In group 5 (EAT+25 mg/kg tomentosin), tumors were seen in the serosa layer of the large intestine tissues (Fig. 5e). In group 6 animals that were given EAT+50 mg/kg tomentosin, tumors were seen in the serosa layer of the large intestine tissues, but the tumor size was determined to be smaller than in Group 5 (Fig. 5f). When the large intestine tissues of the 7th Group animals administered EAT+100 mg/kg tomentosin were examined, it was determined that there were tumor cells in the serosa layer, but their number and size were significantly reduced compared to the other tumor groups (Fig. 5g).

Stomach: The gastric tissues of Group 1 and 3 animals without EAT were normal. The morphology of the gastric cavities, glands, submucosa, muscularis and serosa layers were found to be healthy only in the group given tomentosin (Fig. 6a and c). When the stomach tissues of the animals in the other tumor-treated groups were examined, tumor tissue was observed in the serosa layer of the stomach tissue of the 2nd Group animals (Fig. 6b). In the 4th group (EAT+5-FU), a tumor was found outside the stomach tissues (Fig. 6d). Tumor tissue was observed in the serosa layer of the stomach tissue of the animals in the 5th group (EAT+25 mg/kg tomentosin) (Fig. 6e). Tumor tissue was observed in the serosa layer of the tissue of the 6th Group animals treated with EAT+50 mg/kg tomentosin, but the tumor size was determined to be smaller than the 5th Group (Fig. 6f). When the gastric tissues of the 7th Group animals treated with EAT+100 mg/kg tomentosin were examined, it was determined that tumor cells were present in the serosa layer, but their number and size were significantly reduced compared to the other groups (Fig. 6g).

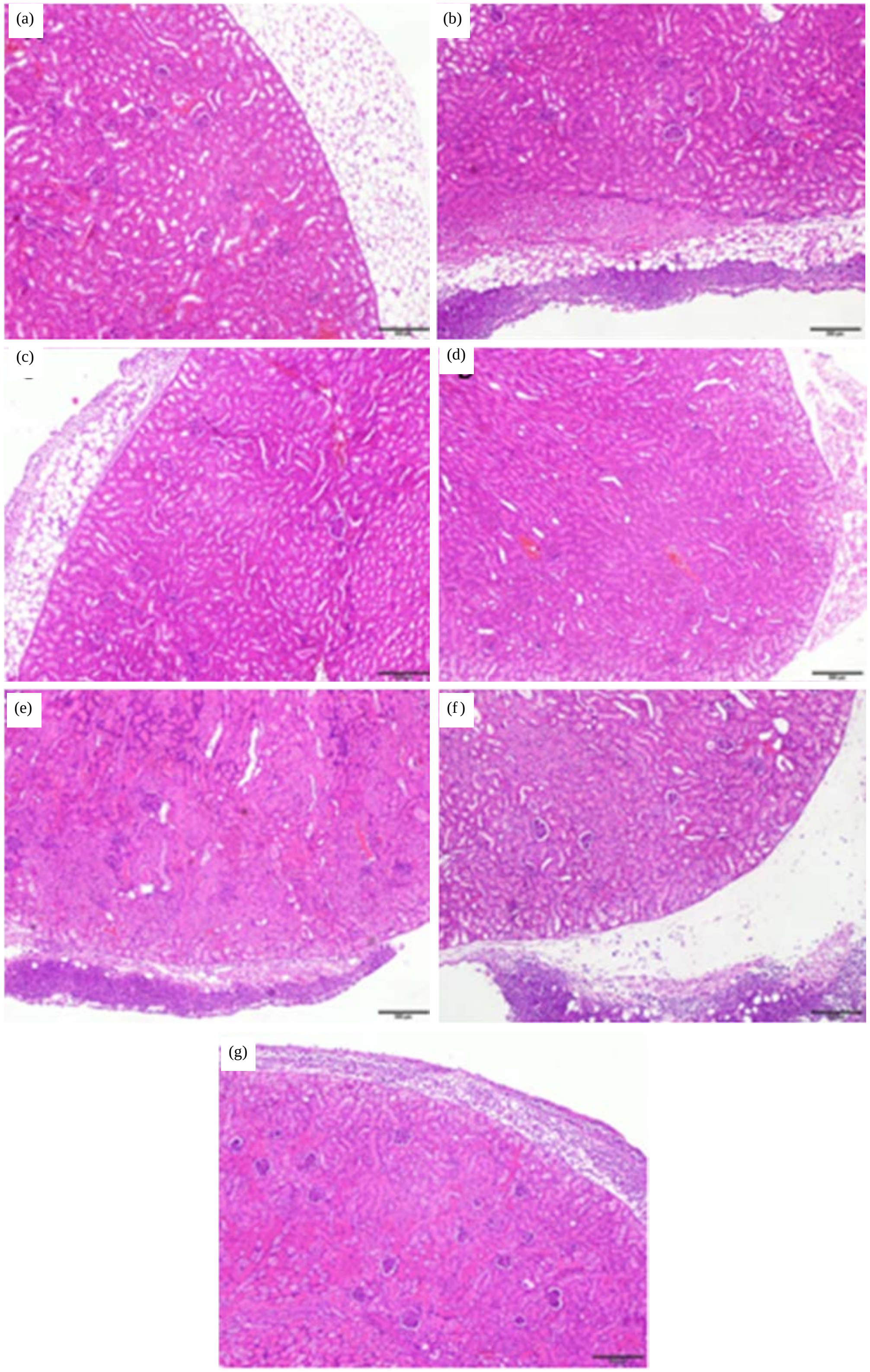

Fig. 3(a-g): Kidney tissues, (a) Healthy kidney tissue, (b) Kidney tissue with EAT, (c) Tomentosin-treated kidney tissue, (d) EAT+5FU treated kidney, (e) EAT+tomentosin (25 mg/kg), (f) EAT+tomentosin (50 mg/kg) and (g) EAT+tomentosin (100 mg/kg)

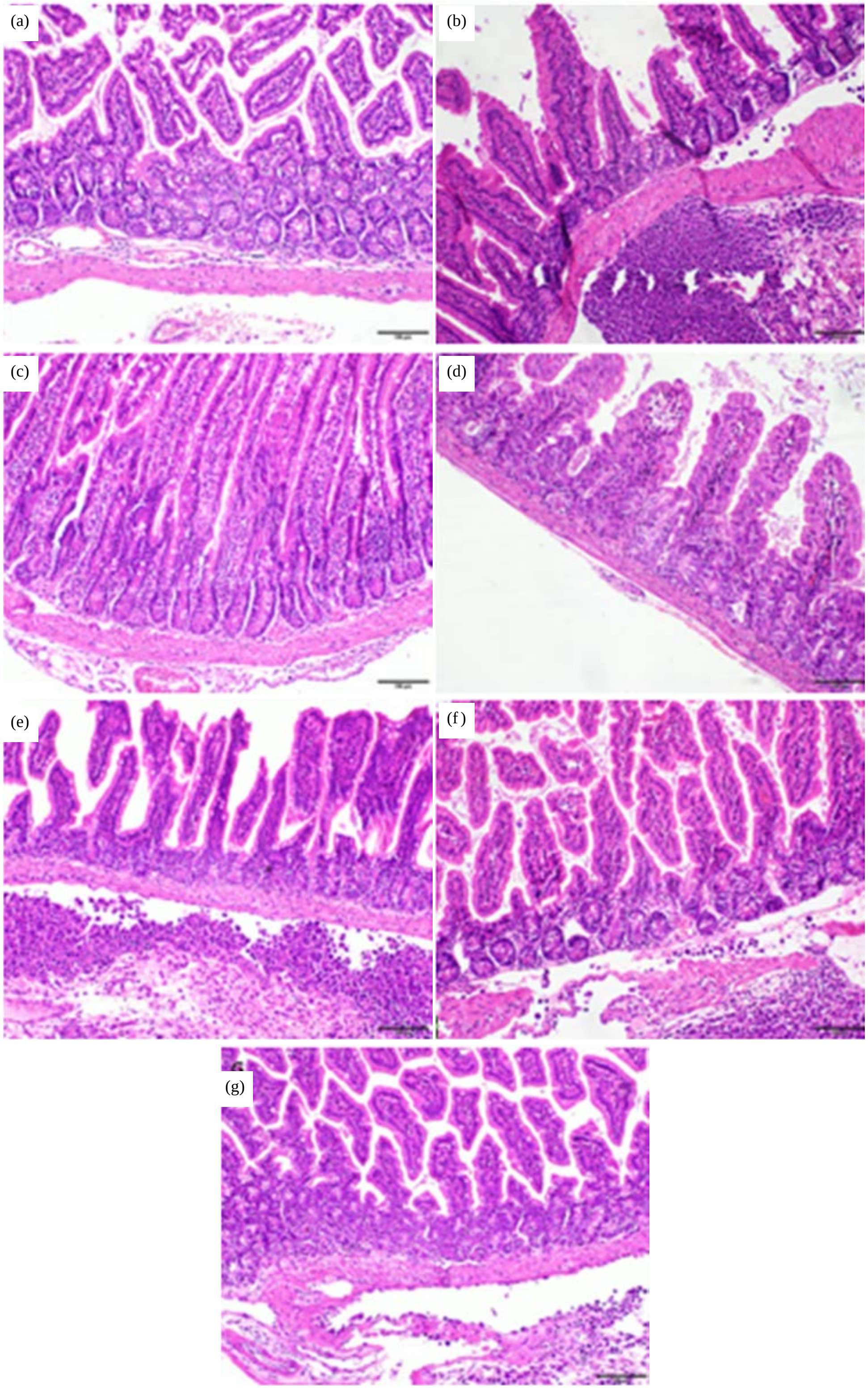

Fig. 4(a-g): Small intestine, (a) Healthy small intestine, (b) Small intestine with EAT, (c) Small intestine treated with tomentosin, (d) Small intestine treated with EAT+5FU, (e) EAT+tomentosin (25 mg/kg), (f) EAT+tomentosin (50 mg/kg) and (g) EAT+tomentosin (100 mg/kg)

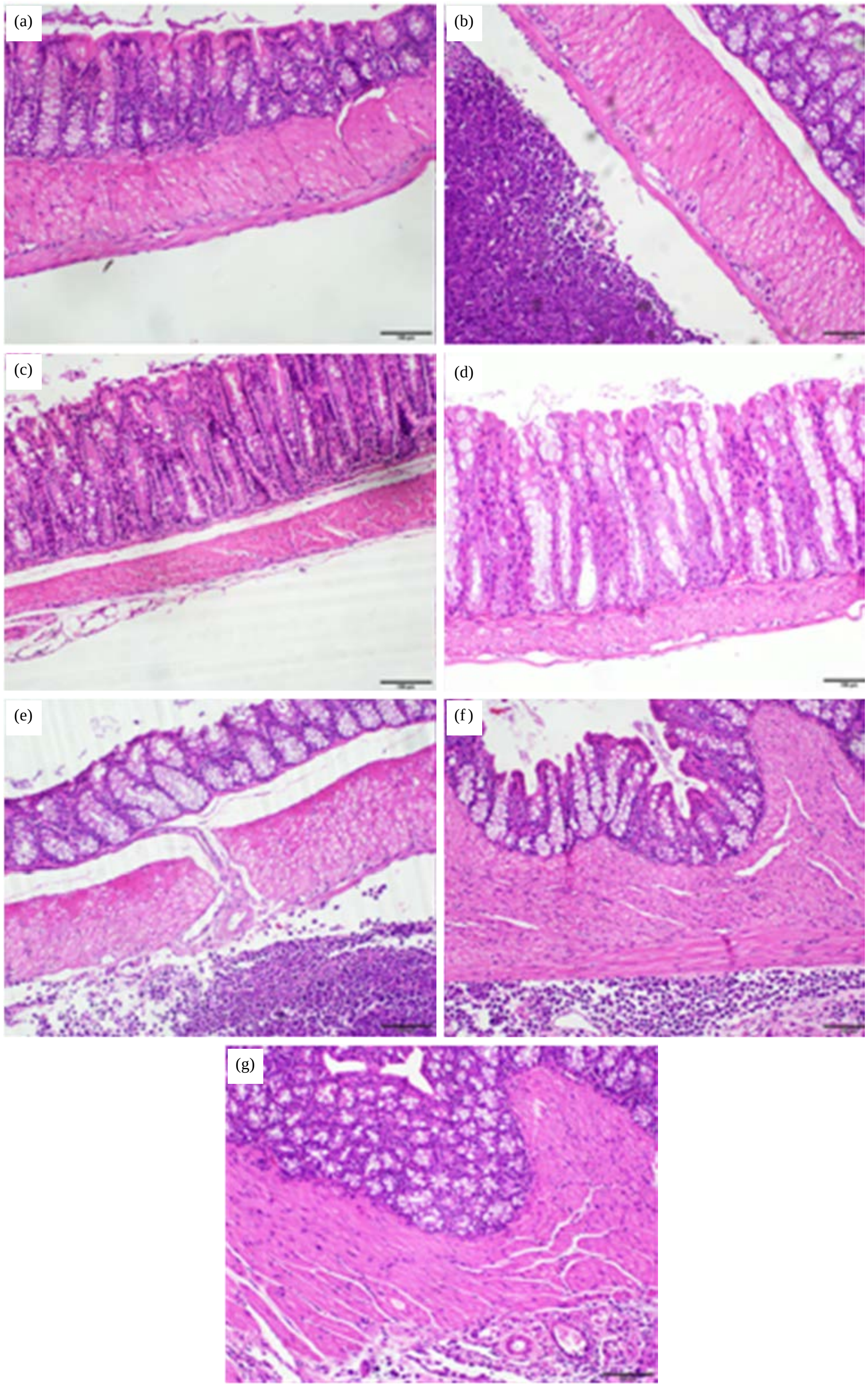

Fig. 5(a-g): Large intestine, (a) Healthy large intestine, (b) Large intestine with EAT, (c) Tomentosin-treated large intestine, (d) Large intestine treated with EAT+5FU, (e) EAT+tomentosin (25 mg/kg), (f) EAT+tomentosin (50 mg/kg) and (g) EAT+tomentosin (100 mg/kg)

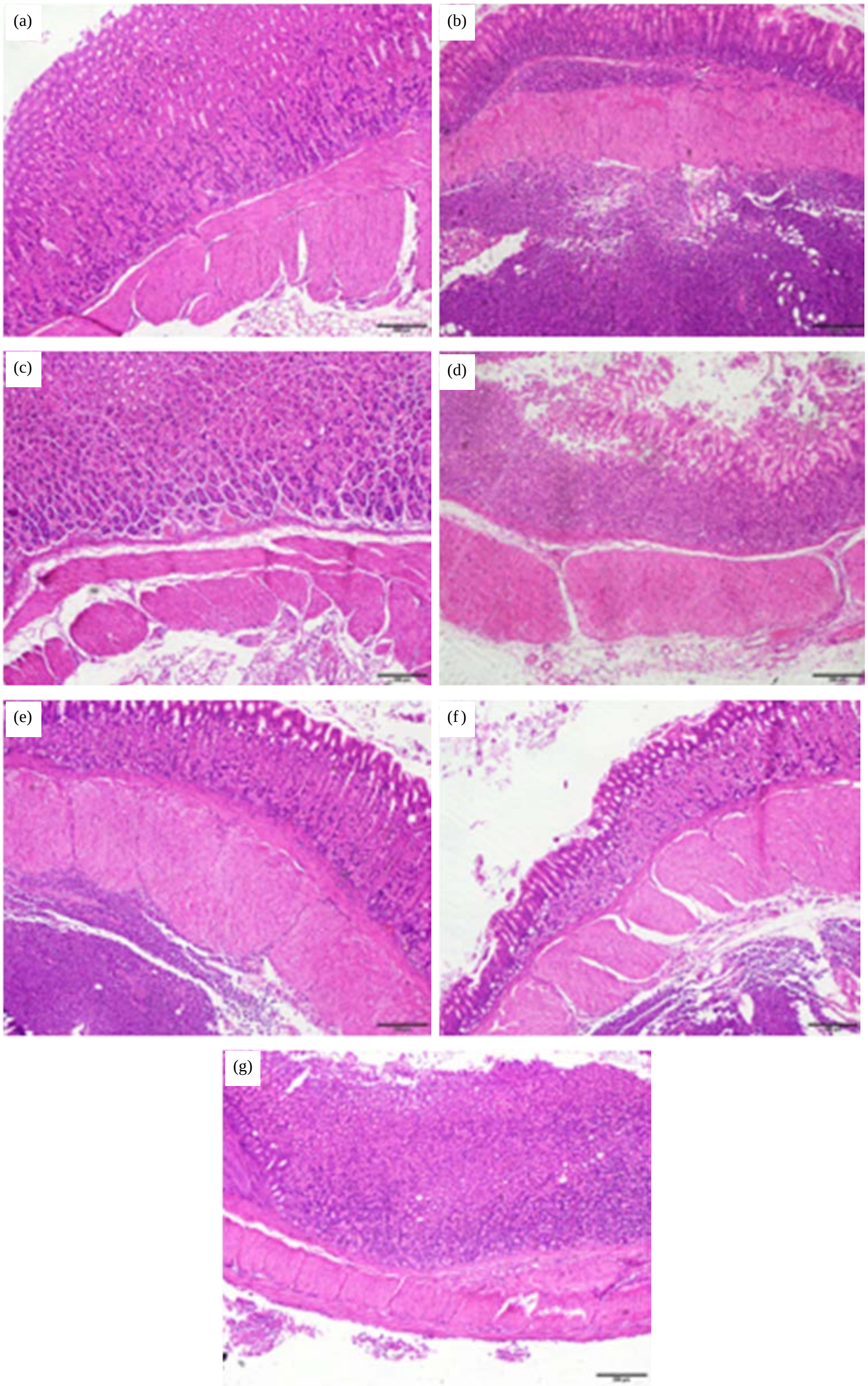

Fig. 6(a-g): Stomach, (a) Healthy Stomach, (b) Stomach with EAT, (c) Tomentosin treated stomach, (d) EAT+5FU treated stomach, (e) EAT+tomentosin (25 mg/kg), (f) EAT+tomentosin (50 mg/kg) and (g) EAT+tomentosin (100 mg/kg)

DISCUSSION

Spontaneously occurring or transferable tumor models are similar to human cancers and play a role in cancer studies. The Ehrlich ascites tumor used in this study, is specific to mice and is an aggressive model that can be easily transferred from one mouse to another, resulting in 100% mortality[2].

In the literature search, *in vivo* studies investigating tomentosin are limited in number. In this respect, the originality of this study and its contribution to the literature is very important.

There are many *in vitro* studies on the anticancer activity of tomentosin, one of the natural sesquiterpene lactones. Aiming to clarify the cytotoxic mechanism of tomentosin in Human Hepatocellular Carcinoma (HCC) cell lines HepG2 and Huh7, the researchers showed that tomentosin decreased the viability and suppressed the proliferation rate of HepG2 and Huh7 cells in a dose- and time-dependent manner by WST-1, cell counting and colony formation assay results. Cell cycle analysis revealed that tomentosin-treated HepG2 and Huh7 cells had increased cell population at SubG1 and G2/M stage and decreased cell population at G0/1 stage[14]. In this study, tomentosin decreased the weight of the tumor load in the animals and histological analysis showed that cell invasion decreased in tomentosin-treated groups. In this respect, this research results are parallel to the studies conducted by Yu *et al.*[14].

In a 2017 study, Merghoub *et al.*[15] observed that tomentosin targeted the telomere mechanism and induced apoptosis in cervical cancer SiHa and HeLa cell lines and suggested that the explanation for this tomentosin-induced apoptosis may be through a mitochondria-mediated signaling.

In a study with tomentosin on multiple myeloma cells, tomentosin was shown to have potent antitumor activity on multiple myeloma cells through inhibition of cell proliferation and induction of cell apoptosis. Furthermore, tomentosin has been reported to induce down-regulation of genes enriched in immune system pathways as well as pathways that promote proliferation, growth, migration and invasion. Tomentosin is thought to inhibit the growth of multiple myelomas through induction of apoptosis by upregulation of the PERK/eIF2a/ATF4/DDIT3 pathway[16].

When the TAS results were evaluated in this study, there was an increase in TAS capacity with the increase in the dose of tomentosin between the groups in which EAT and tomentosin were given together (Table 3). In a study on human Burkitt lymphoma cells, tomentosin was found to be a powerful antioxidant due to its inhibition of cell proliferation and induction of apoptosis[17]. Results are similar to this study.

In an *in vitro* study investigating the anticancer activity of tomentosin using PANC-1 and MIA PaCa-2 human pancreatic cancer cells, it was revealed that tomentosin stimulates apoptosis, reduces migration, invasion and colony forming abilities[18].

The body weight of mice with Ehrlich ascites tumors is expected to increase over time depending on the number of cells and the volume of ascites fluid. In a 2008 study, Curcumin analogs 3a and b were used against Ehrlich ascites tumor and a decrease in average body weight was observed in curcumin-treated groups due to decreased tumor burden compared to the increased body weight of control mice[19]. According to the data obtained at the end of this study, a decrease in mean body weight was observed in the tumor and tomentosin co-treated groups compared to the control group due to decreased tumor burden (Fig. 2). In this respect, study is consistent with the study by Chandru *et al.*[19]. Therefore, tomentosin was found to be effective against tumor burden.

A 2014 study showed that tomentosin has anti-inflammatory activity through inhibition of inflammatory mediators by regulating NF-κB activation and phosphorylation of p38/JNK kinases[20].

Tomentosin shows anticancer effects by inducing ROS-induced MMP (mitochondrial membrane potential). Furthermore, inhibition of NF-κB activation via the mTOR/PI3K/AKT pathway leads to apoptosis in MOLT-4 human leukemia cells[8]. A 2019 study with human osteosarcoma MG-63 cells showed that tomentosin induced apoptosis in MG-63 cells and increased intracellular ROS levels, important mediators of apoptosis and decreased cell viability and migration ability in MG-63 cells[21]. In a study investigating the anticancer properties of tomentosin in AGS gastric cancer cells, it was determined that tomentosin had a cytotoxic effect and caused ROS formation[22]. In this study, it was determined that tomentosin applied against the EAT model increased the level of SOD, an antioxidant enzyme. In this respect, the current study supports these studies.

When the TOS results were analyzed, the results obtained were not consistent with the literature. When the same study was re-run very carefully, reviewing all materials and methods, the results did not change.

In a 2021 study conducted by Zhang *et al.*[23], they used tomentosin against DMBA-induced breast cancer in rats and showed that tomentosin effectively reduced alpha receptor levels, cytokinin levels and oxidative stress markers. As a result of histological analysis on breast tissue, the researchers determined that tomentosin effectively prevented DMBA-induced damage in this tissue. When this study was evaluated histologically, it was seen that 100 mg/kg dose of tomentosin reduced tumor development against tumors in kidney, small intestine, large intestine and stomach tissues compared to 25 and 50 mg/kg doses and only the tumor group. Therefore, this study supports the study of Li *et al.*[23].

In a study investigating the anticancer activity of tomentosin on SK-28, 624 and 1363 mel melanoma cells, it was reported to inhibit proliferation and induce cell cycle arrest[24].

In a study investigating the anticancer effect of tomentosin on U87 human GBM (Glioblastoma Multiforme) cells, it was concluded that tomentosin increased the expression of BAX, CASP3, CASP8, CASP9, CYCS, FADD, TNF, TNFR1, TNFR2 and TIMP2 genes and significantly reduced the colony forming capacity of U87 cells. Tomentosin is thought to exert its anticancer effect by altering the expression levels of apoptosis and metastasis-related genes in U87 GBM cells[25].

The current study shows similar characteristics to the studies conducted in this field in terms of reducing tumor burden, increasing total antioxidant capacity, increasing superoxide dismutase enzyme activity and preventing tumor invasion when histologically evaluated.

CONCLUSION

Conclusively, it was determined that, according to the weight changes in mice depending on the tumor load, a 100 mg/kg dose of tomentosin prevented the proliferation and spread of the tumor compared to other doses and control groups. When biochemical evaluations were taken into consideration, it was concluded that the dose of tomentosin increased the SOD level and improved the defense system. It was also observed that tomentosin increased the antioxidant level depending on the dose. In histological analysis, it was seen that there was tumor involvement in the kidney, small intestine, large intestine and stomach in the tumor model created with EAT and this involvement was observed in the serosa, especially in the peripheral parts of the organs and sometimes in the muscularis and submucosa layers. Morphologically, it was determined that the tumor size decreased in the groups given tomentosin together with the tumor and this decrease was related to the increase in the tomentosin dose. As a result, weight, biochemical and histological evaluations supported each other in that tomentosin reduces the tumor and it is thought that current study will help future studies.

SIGNIFICANCE STATEMENT

In the study, tomentosin was applied in 3 doses: 25, 50 and 100 mg/kg. Tomentosin demonstrated significant tumor-suppressive effects in the EAT mouse model, particularly at a dose of 100 mg/kg. The dose-dependent reduction in tumor size, supported by biochemical and histopathological findings, highlights its potential as a chemo-suppressive agent. These results contribute to the growing evidence supporting plant-derived compounds in cancer therapy. It also shows that tomentosin is promising as a potential agent in cancer treatment and deserves further investigation.

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