ORIGINAL ARTICLE

Is there any effect of lycopene's preventing peritoneal adhesion formation in rats: an experimental study

¿Tiene el licopeno algún efecto en la prevención de la formación de adherencias peritoneales en ratas? Un estudio experimental

Ahmet Bilgi[1], Mustafa C. Terek[2], Gürkan Yiğittürk[3], Dilek Taşkıran[4], Orkun İlgen[5], İsmet Hortu[2], Bulent Yilmaz[6], Cavit Kart[7], Fazıl Avcı[1], and Mehmet Kulhan[1]*

[1]Department of Gynecology and Obstetrics, Selçuk University Faculty of Medicine, Konya; [2]Department of Gynecology and Obstetrics, Ege University Faculty of Medicine, Izmir; [3]Department of Histology and Embryology, Mugla Sitki Kocman University Faculty of Medicine, Mugla; [4]Department of Physiology, Ege University Faculty of Medicine, Izmir; [5]Department of Gynecology and Obstetrics, Dokuz Eylul University Faculty of Medicine, Izmir; [6]Department of Gynecology and Obstetrics, Recep Tayyip Erdogan University Faculty of Medicine, Rize; [7]Department of Gynecology and Obstetrics, Karadeniz Technical Unıversity Faculty of Medicine, Trabzon. Turkey

Abstract

Objective: *Effects of lycopene in prevention of intra-abdominal adhesion formation in a rat model.* **Methods:** *Twenty-eight rats were divided into four groups consisting of 7 rats each. Group 1 (only adhesion), Group 2 (adhesion + corn oil), Group 3 (adhesion + 5 mg/kg lycopene), Group 4 (adhesion + 20 mg/kg lycopene). Adhesion score, histopathology, vascular endothelial growth factor (VEGF) H-score, malondialdehyde (MDA), total antioxidant capacity, and VEGF values were measured.* **Results:** *There were significantly higher extent, severity, degree, and total adhesion scores in the control and corn-oil group than in the low lycopene and high lycopene group. VEGF H-scores were significantly lower in lycopene-given groups, regardless of dose. When the low lycopene and high lycopene groups were compared in terms of anti-VEGF H-score, no significant difference was observed. Malondialdehyde levels were statistically significantly lower in the control and high lycopene group.* **Conclusions:** *Biochemical parameters, histopathological examination, and adhesion scoring revealed that lycopene significantly reduced adhesion formation.*

Keywords: *Adhesion. Lycopene. Peritoneum. Rat. Vascular endothelial growth factor.*

Resumen

Objetivo: *Evaluar los fectos del licopeno en la prevención de la formación de adherencias intraabdominales en un modelo con ratas.* **Métodos:** *Veintiocho ratas se dividieron en cuatro grupos de siete cada uno: grupo 1, solo adhesión; grupo 2, adhesión más aceite de maíz; grupo 3, adhesión más 5 mg/kg de licopeno; y grupo 4, adhesión más 20 mg/kg de licopeno. Se midieron la puntuación de adherencia, la histopatología, la puntuación H del factor de crecimiento endotelial vascular (VEGF), el malondialdehído, la capacidad antioxidante total y los valores de VEGF.* **Resultados:** *Hubo puntuaciones de extensión, gravedad, grado y adhesión total significativamente más altas en los grupos control y con aceite de maíz que en el grupo con bajo y alto licopeno. Las puntuaciones VEGF H fueron significativamente más bajas en los grupos que recibieron licopeno, independientemente de la dosis. Cuando se compararon los grupos con niveles bajos y altos de licopeno en términos de puntuación H anti-VEGF, no se observaron diferencias significativas. Los niveles de malondialdehído fueron más bajos en los grupos de control y alto en licopeno, con una diferencia estadísticamente significativa.* **Conclusiones:** *Los parámetros bioquímicos, el examen histopatológico y la puntuación de adherencias revelaron que el licopeno redujo significativamente la formación de adherencias.*

Palabras clave: *Adhesión. Licopeno. Peritoneo. Rata. Factor de crecimiento endotelial vascular.*

Correspondence:
Fazıl Avcı
E-mail: fazilavci01@hotmail.com

Date of reception: 12-08-2024
Date of acceptance: 06-11-2024
DOI: 10.24875/CIRU.24000434

Cir Cir. 2026;94(3):293-300
Contents available at PubMed
www.cirugiaycirujanos.com

Introduction

Although our knowledge about peritoneal cavity physiology and peritoneal healing mechanisms is increasing, post-operative adhesions continue to be a problem for surgeons from different disciplines. In different studies, the direct relationship between intra-abdominal surgical interventions and adhesion formation has been revealed, and it has been stated that the most important cause of intestinal obstruction is adhesions due to previous surgeries.[1,2] Post-operative adhesions are fibrous connections that can be seen between organs that are not normally combined with each other and are surrounded by serous membranes following injury or surgical operations.[1] Approximately 30% of intestinal obstructions develop due to intra-abdominal adhesion, and post-operative peritoneal adhesion occurs in more than 90% of all laparotomies. In addition, they may lead to post-operative mortality, morbidity, and cost increase due to their ability to extend the length of hospital stay.[3] Despite advanced surgical techniques and medical treatment options, post-operative intra-abdominal adhesions are still an unsolved problem. When the literature is searched, it is seen that many experimental, clinical studies, and theoretical reports on adhesion prevention have been published since the beginning of the century. Various chemical agents used as adhesion inhibitors prevent fibrin organization by inhibiting fibroblastic proliferation. Therefore, many agents such as non-steroidal anti-inflammatory drugs, corticosteroids, calcium channel blockers, histamine antagonists, antibiotics, fibrinolytic drugs, antioxidants, and vitamins have been tried to inhibit this proliferation.[4] Lycopene is a pigment belonging to the carotenoid family, naturally found in vegetables and fruits. Lycopene is a potent antioxidant substance; besides protecting cells from free radical damage, it strengthens the bonds between cells and improves cell metabolism.[5-10] There have been reports supporting lycopene's effect on reduced risk of many diseases, including Alzheimer's disease, peripheral nerve damages,[11] cardiovascular disease, skin health,[12,13] and even some types of cancer (breast and uterine).[14] Lycopene also slows down the aging process with its antioxidant properties.[15] In this observational rat study, we investigated the effectiveness of lycopene use in preventing adhesions after gynecological surgery.

Methods

Ethical statement

This study was approved by our University Animal Experiments Local Ethics Committee (April 26, 2017, Protocol No: 2017/011).

Study design

Twenty-eight female Wistar albino rats were included in the study. Inclusion criteria in the study were as follows: the animals were female Wistar albino species, weighing between 160 and 250 g, and survived from the beginning to the end of the study. The exclusion criteria were as follows: the animals were out of the female Wistar albino species, their weight was not between 160 and 250 g, and they died before the study was completed. Experimental animals were kept in our University Animal Laboratory at a room temperature of 24°C and a 12/12 h day and night cycle. Fed with standard rat food and water without restrictions. Each rat was anesthetized with ketamine hydrochloride (40 mg/kg IV). Before surgery, the abdominal area of the rats was shaved and wiped with 1% povidone iodine and prepared for the operation. Approximately 4 cm lower midline laparotomy was performed on the umbilical region. Before surgery, the rats were randomly divided into four groups each consisting of 7 rats. The operations performed on groups of rats were as follows:

- Control group (CG): a standard adhesion was created; no adjuvant was given. Corn oil group (CoG): After the injury, 1 mL of corn oil was administered daily by direct intraperitoneal injection method. The same dose was continued intraperitoneally for 14 days
- Low-dose lycopene group (LLG); After the injury, 5 mg/kg lycopene was administered daily by direct intraperitoneal injection method. The same dose was continued intraperitoneally for 14 days
- High-dose lycopene group (HLG): After injury, only a single dose of 20 mg/kg lycopene was administered intraperitoneally.

Lycopene is a powder compound. It has been used in a liquid-based substance, corn oil, to make lycopene suitable for intraperitoneal injection. To determine the effect of corn oil alone, the CoG was created as a separate group. The dose of lycopene was chosen based on a previous study.[16]

After a 4 cm abdominal incision, the uterine horns were exposed and a lesion was created on the antimesenteric surface of each uterine horn (free part of the bicornual rat uterus in the pelvic area) surface with the help of a 10-volt bipolar cautery as previously described.[17] At the same time, extra adhesion was created by scraping operations on the visceral surface until serosal bleeding occurred. After the procedure was completed, the abdomen was closed continuously using 4.0 Vicryl. The rats were then allowed to recover for 2 weeks. A total of 4 animals died of lung infection before starting the experiment. Animals that died were excluded from the study. After the recovery period, the animals were sacrificed and evaluated for adhesion formations. The researchers who evaluated the adhesions had no prior knowledge of which group the rat belonged to. Adhesion scoring based on extent, severity, and resistance to applied force is summarized in table 1.[18,19]

The sum of the three parameters was used as the total score for each group. Tissue samples taken from the peritoneum and adhesion area were sent for histopathological examination. Adhesion examples are shown in figure 1.

Table 1. Macroscopic adhesion scoring method

Score	Extend	Severity	Degree
0	No	No	No
1	< 25%	Filmy avascular	Detached with gentle traction
2	Between 25 and 50%	Opaque, translucent, avascular	Detached with moderate traction
3	Between 50 and 75%	Vascular or opaque	Detached with sharp traction
4	More than 75%	Opaque, thick veins available	-

The adhesion score is equal to the sum of the scores from each part of the adhesion. The highest possible score is 11

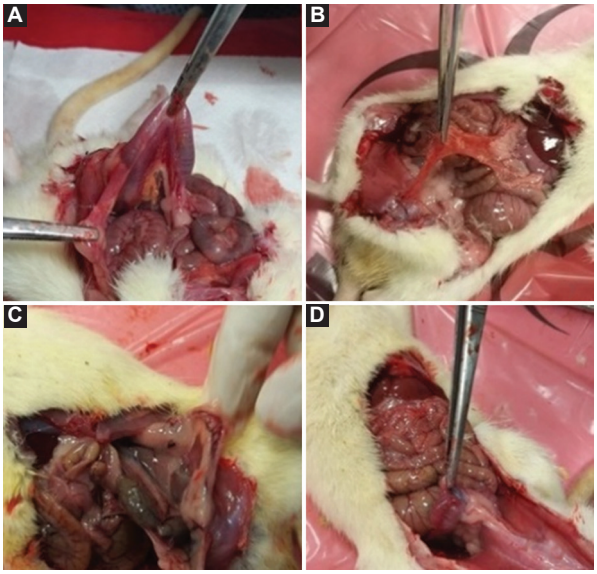

Figure 1. *Adhesion examples.* **A:** *adhesions between bowel and uterine horn.* **B:** *fibrous adhesion between bowel and uterine horn.* **C** *and* **D:** *complete adhesion to the anterior abdominal wall and bowel.*

Histopathological examination

Tissues were fixed with formaldehyde for 48 h and washed with phosphate-buffered saline at pH 7.4. Dehydration was achieved by passing the tissues through increasing concentrations of ethyl alcohol (from 80%, 90%, 90%, 96% and to 96%) for 45 min in each ethanol series. After dehydration, specimens were cleared in xylene and embedded in paraffin wax.[20] Paraffin tissue blocks (5-μm thickness) were cut using a rotary microtome. Tissue sections were stained with hematoxylin and eosin staining for histomorphological analysis.[21] Tissue slides were visually assessing with a Nikon Eclipse 80i image analysis system. A total of 100 fields were scored per tissue in 10 random slide of view taken with a ×10 objective for evaluation of tissue inflammation and edema.

Anti-vascular endothelial growth factor (VEGF) ımmunohistochemical staining

For immunohistochemistry (IHC), sections were incubated with H_2O_2 (3%) for 30 min to eliminate endogenous standard activity and blocked with protein block for 20 min at room temperature. Later, sections were incubated with primary antibody (anti-VEGF, Santa Cruz Biotechnology, Inc.; dilution 1/100) overnight at 4°C. Antibody detection was performed with the UltraTek HRP Anti-Polyvalent Staining System (ScyTec Inc., USA), and 3,30-diaminobenzidine was used to visualize the final product.[22]

Immunostaining was evaluated semiquantitatively using H-score analysis. Immunostaining intensity was categorized under the following scores: 0 (no staining), 1 (weak staining), 2 (moderate staining), and 3 (intense staining). H-score value was derived for each specimen by calculating the sum of the percentage of cells for the cytoplasmic and nuclear immunoreaction

of the sections that were stained at each intensity category multiplied by its respective score, by means of the formula H-score = ΣPi (i + 1), where i = intensity of staining with a value of 1, 2, or 3 (weak, moderate, or strong, respectively) and Pi is the percentage of stained cells for each intensity, varying from 0% to 100%. For each slide, 10 different fields were microscopically evaluated at ×20 magnification. H-score evaluations were independently performed by at least two investigators blinded to the source of the samples as well as to each other's results.

Biochemical analysis

Measurement of lipid peroxide level

Measurement of lipid peroxides in tissue samples was made by the Uchiyama and Mihara methods.[23] Malondialdehyde (MDA) levels in the samples were calculated from the calibration curve prepared from standard solutions. Results are given as nmoL/mg protein.

Measurement of VEGF level

Measurement of VEGF levels in tissue samples was carried out with an enzyme-linked ımmunosorbent assay (ELISA) kit (Sun Red, Shanghai Sunred Biological Technology Co. Ltd.). First of all, standard samples were prepared. Standard prefixes of 50, 100, 200, 400, 800, and 1600 ng/L were prepared from the stock solution. 0.05 mL standard and 0.05 mL HRP-streptavidin were added to the wells determined in the ELISA plate. Samples were pipetted. The plate was covered and incubated at 37°C for 90 min. For tissue samples, 0.04 mL of sample, 0.01 mL VEGF antibody, and 0.05 mL of the HRP-streptavidin were added. The ELISA plate was incubated at 37°C for 60 min. At the end of the period, all samples were removed from the ELISA plate with a pipette and washed 3 times with washing buffer. At the end of the washing process, chromogen A (0.05 mL) and B solutions (0.05 mL) were added to the wells, and the plate was incubated at 37°C for 15-30 min. At the end of the period, the reaction was stopped by adding 0.05 mL of stop solution to the wells. The optical density of the resulting yellow color was read in a microplate reader (Thermo Scientific® Multiskan Go) at 450 nm wavelength. Results were evaluated according to the standard calibration curve.

Measurement of total antioxidant capacity (TAC)

Measurement of TAC in tissue samples was performed spectrophotometrically with a commercial kit (Rel Assay Diagnostics). According to the principle of this method, the antioxidant molecules in the studied sample cause the formation of a lighter colored compound by reducing the dark blue-green colored ABTS radical. The absorbance of the resulting color is read in the spectrophotometer at a wavelength of 660 nm.[24] The level of antioxidant molecules in the sample is calibrated with the stable antioxidant compound Trolox Equivalent (a vitamin E analog) present in the kit.

Statistical analysis

The Statistical Package for the Social Sciences 25 (SPSS 25) (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp. The statistical package program was used to evaluate the data. Histopathological changes between experimental groups were analyzed comparatively. Experiments were done independently in 6 replicates. Variables are expressed using mean ± standard deviation, percentage, and frequency values. Variables were evaluated after checking the preconditions for normality and homogeneity of variances (Shapiro Wilk and Levene test). For comparison of three or more groups, the one-way ANOVA test and the Tukey Honestly Significant Difference test, one of the multiple comparison tests, were used. For the significance level of the tests, $p < 0.05$ and $p < 0.01$ values were accepted.

Results

The results obtained from the present study are shown in table 2. The total adhesion scores were 5.86 ± 1.21 for the CG, 6.29 ± 1.49 for the CoG, 2.6 ± 1.14 for the LLG, and 2 ± 1.41 for the HLG. There were statistically significant differences between macroscopic adhesion scores between groups. A statistically significant decrease was found in all adhesion scores in rats given lycopene compared to groups not given lycopene, regardless of dose. There were significantly higher extent ($p < 0.05$), severity ($p < 0.05$), degree ($p < 0.05$), and total adhesion ($p < 0.05$) scores in the CG and CoG than in the LLG

Table 2. Macroscopic adhesion score, biochemical, histopathological findings, and VEGF H-score results

Variable	Mean ± standard deviation				p*	p**
	CG	CoG	LLG	HLG		
VEGF (ng/L)	283.75 ± 69.88	351.42 ± 96.47	313 ± 45.4	295 ± 86.44	p = 0.427	
TAC (mmoL trolox Eq/L)	0.77 ± 0.32	0.58 ± 0.13	0.68 ± 0.37	0.74 ± 0.32	p = 0.636	
MDA (nmoL/mL)	13 ± 3.82[a]	20.48 ± 5.29[a, b]	16.08 ± 4.27	11.47 ± 1.47[b]	p = 0.005***	p^a = 0.014*** p^b = 0.007***
Adhesion score						
Extend	2.71 ± 0.48[b,c]	2.85 ± 0.37[d,e]	1.4 ± 0.54[c,d]	1.4 ± 0.54[b,e]	p = 0.000***	p^b = 0.001*** p^c = 0.001*** p^d = 0.001*** p^e = 0.001***
Severity	1.71 ± 0.48[b]	2 ± 0.81[d,e]	0.8 ± 0.44[d]	0.4 ± 0.54[b, e]	p = 0.001***	p^b = 0.007*** p^d = 0.015*** p^e = 0.001***
Degree	1.42 ± 0.78[b]	1.42 ± 0.78[e]	0.4 ± 0.54	0.2 ± 0.44[b,e]	p = 0.007***	p^b = 0.029*** p^e = 0.029***
Total	5.85 ± 1.21[b,c]	6.28 ± 1.49[d,e]	2.6 ± 1.14[c,d]	2 ± 1.41[b,e]	p = 0.000***	p^c = 0.002*** p^b = 0.000*** p^d = 0.001*** p^e = 0.000***
Histopathological findings and VEGF H-score						
Inflammation	4.21 ± 1.3	4.01 ± 2.30	3.9 ± 1.36	1.10 ± 2.1[f]		p^f = 0.005***
Edema	2.42.0 ± 2.2	2.33 ± 0.26	2.212 ± 0.72	0.11 ± 0.64[f]		p^f = 0.002***
VEGF H-Score	271.30 ± 2.41	265.12 ± 0.96	152.23 ± 1.10[g]	132.56 ± 1.12[g]		p^g = 0.01***

*Data were analyzed using one-way ANOVA test.
**Data were analyzed using the Tukey HSD test.
***p-value was considered statistically significant.
p^a: comparison between CG and CoG.
p^b: comparison between CG and HLG.
p^c: comparison between CG and LLG.
p^d: comparison between CoG and LLG.
p^e: comparison between CoG and HLG.
p^f: comparison between CG, CoG, and LLG.
p^g: comparison between CG and CoG.
CG: control group; CoG: corn oil group; LLG: low lycopene group; HLG: high lycopene group; VEGF: vascular endothelial growth factor; TAC: total antioxidant capacity; MDA: malondialdehyde.

and HLG. Although some adhesion scores (severity, degree, and total adhesion score) were lower in the HLG compared to the LLG, these differences were not statistically significant. P-values were 0.73, 0.97, and 0.89, respectively. There was no significant difference between the CG and CoG in terms of all scoring. The line charts of the groups according to the adhesion score are shown in figure 2.

When histopathological findings are evaluated, a high level of inflammation was observed between the perimetrium and smooth muscles in the CG and CoG groups. Hyperemia and intense inflammatory cells have been detected in vascular structures. Moderate edema and thickening were also detected in the perimetrium. Similar to CG and CoG groups, high-level inflammation, hyperemia, and moderate edema were observed in the

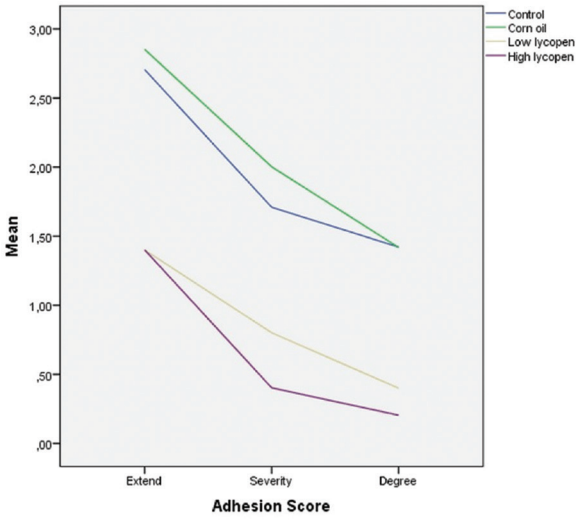

Figure 2. *Line charts according to the adhesion score of the groups.*

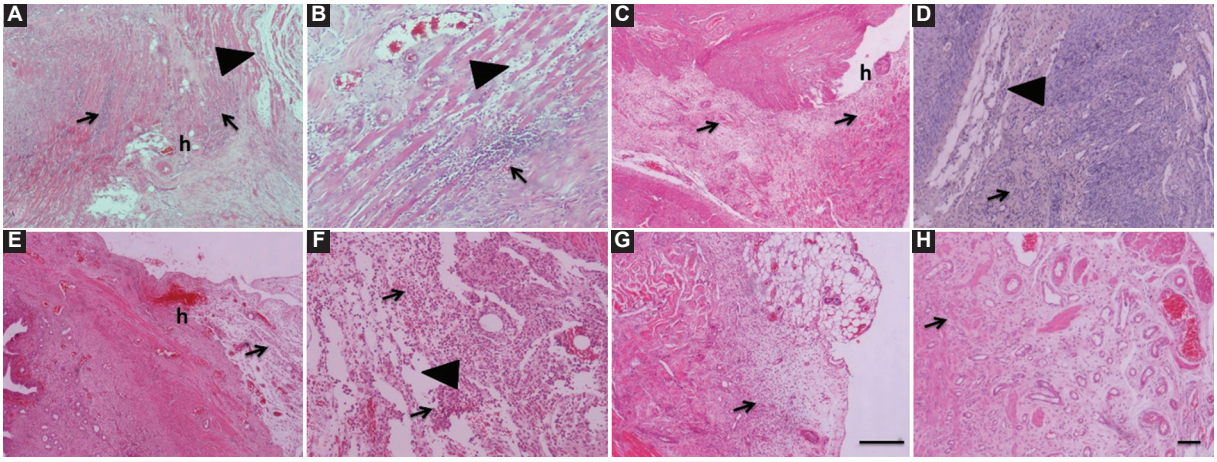

Figure 3. A: *control group (CG), black arrow; high level of inflammation in the perimetrium and between smooth muscles, arrowhead; moderate edema, h; hyperemia magnification ×4.* **B***: CG black arrow; high level of inflammation in the perimetrium and between smooth muscles, arrowhead; moderate edema, magnification ×10.* **C***: corn oil group (CoG), black arrow; high level of inflammation in the perimetrium and between smooth muscles, h; hyperemia magnification ×4.* **D:** *CoG arrowhead; moderate edema, magnification ×10.* **E***: low-dose lycopene group (LLG), black arrow; high level of inflammation in the perimetrium, h; hyperemia magnification ×4.* **F***: LLG black arrow; high level of inflammation in the perimetrium, arrowhead; medium edema magnification ×10,* **G***: high-dose lycopene group (HLG) black arrow; low level inflammation in the perimetrium ×4.* **H***: HLG black arrow; low-level inflammation in perimetrium, magnification ×10, hematoxylin and eosin staining.*

perimetrium in the LLG. Inflammation ($p = 0.005$) and edema ($p = 0.002$) decreased statistically significantly ($p < 0.05$) in the HLG group compared to the other groups, including the LLG group. Symptoms of hyperemia almost disappeared (Table 2 and Fig. 3).

Anti-VEGF involvement was observed around the vascular structures and perimetrium in the anti-VEGF IHC staining of the uterine sections of the experimental groups. It was observed that VEGF H-score values of the CG and CoG groups were statistically significantly different from LLG ($p = 0.01$) and HLG ($p = 0.01$) groups ($p < 0.05$). VEGF H-scores were significantly lower in lycopene-given groups, regardless of dose. When LLG and HLG were compared in terms of anti-VEGF H-score, no significant difference was observed (Table 2 and Fig. 4). There was no significant difference between the groups in terms of VEGF and TAC in biochemical parameters except for MDA (Table 2). Compared to the CoG group, MDA levels were statistically significantly lower in the CG and HLG ($p < 0.05$). Line charts of the results of biochemical TAG, MDA, and VEGF markers according to the groups are shown in figure 5.

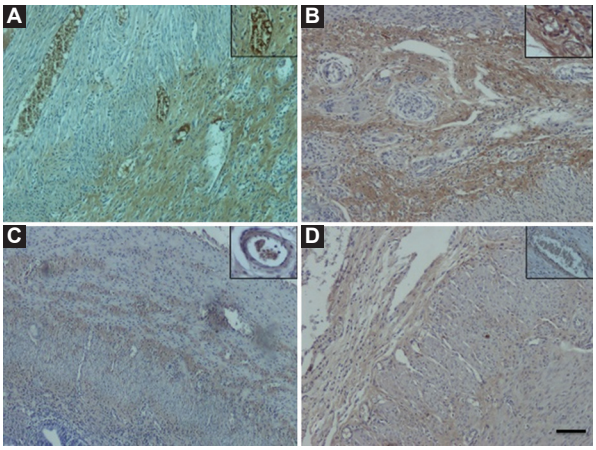

Figure 4. *Anti-vascular endothelial growth factor immunohistochemical staining.* **A***: control group.* **B:** *corn oil group.* **C:** *low-dose lycopene group.* **D:** *high-dose lycopene group, magnification of large pictures is ×10, thumbnails represent vascular structures belonging to groups.*

Discussion

Post-operative adhesions are a result of the cellular and biochemical response that occurs after peritoneal trauma while attempting to repair the peritoneum. Many methods have been used to reduce adhesion formation, such as reducing the initial inflammatory response, preventing fibrin formation, increasing fibrinolysis, preventing collagen deposition, and using a barrier against adhesion formation, and many studies have been conducted on them[25] but today there is still no drug or method that can be used alone that can prevent adhesion formation satisfactorily. Many studies have shown that inflammatory cells and reactive oxygen species play a role in the formation of adhesion. The anti-adhesion effects of antioxidants have been tested in various animal models.[26] Heparin application before and after the operation has been shown

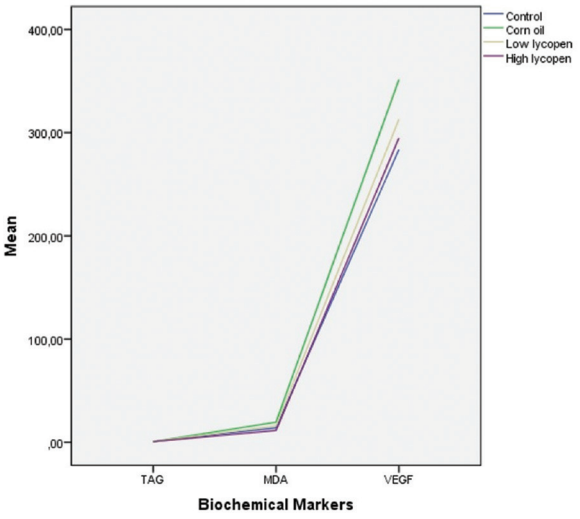

Figure 5. *Line charts of the results of biochemical TAG, MDA, and VEGF markers according to groups. MDA: malondialdehyde; TAC: total antioxidant capacity and VEGF: vascular endothelial growth factor.*

to have anti-adhesive efficacy in a rat adhesion model made by Başbuğ et al.[27] In another anti-adhesion model with quercetin, the adhesion scores of the Quercetin + Surgicel group were reported to be lower than the quercetin group.[17] In this study, we tried to examine the potential effect of lycopene, a potent antioxidant, antiproliferative, anticarcinogenic, and anti-inflammatory, on adhesion formation in rats with traumatized uterine serosa.[15] To our knowledge, the present study is the first study that used lycopene as an adhesion inhibitor in an animal model.

MDA is produced by cells involved in the inflammatory response. It is a by-product formed by oxygen radicals breaking down lipid-containing structures such as plasma and cell membranes. It is a parameter used in evaluating both tissue damage and inflammation severity.[28] In our study, a significant difference was observed between the HLG and CG in terms of MDA levels ($p = 0.007$). Although MDA levels were found to be lower in the HLG than in the LLG, this difference was not statistically significant.

VEGF is an angiogenic cytokine that participates in the process of adhesion formation through the formation of new vessels.[29] In this study, although there was no statistical difference between the groups in terms of VEGF release, numerically, more VEGF-positive cells were encountered in the treatment groups compared to the CG. We think that the biochemical and histopathological VEGF analysis differences between the experimental groups are due to the difference in the number of samples evaluated statistically.

Substances that prevent oxidation caused by free radicals and have the ability to capture and stabilize free radicals are called “antioxidants.” The total effect of all antioxidants in body fluids is called total TAC.[30] In this study, there was no significant difference between the groups in terms of TAC. Higher TAC levels were detected in the HLG but it was statistically insignificant.

Various methods have been used for grading intra-abdominal adhesions. The systems that are made according to the percentage of traumatized adherent area used by Linsky et al.[31] and Leach et al.[18] systems, consisting of three different parameters, are the most commonly used methods.[31] We used the system of Leach et al.[18] In this system, adhesions are scored in three separate categories according to type, prevalence, and easy or difficult separation. In our study, adhesion scores were significantly lower in the lycopene groups compared to the CG, which indicates the effectiveness of lycopene alone in reducing adhesion formation, in line with other studies.[32] In *in vitro* studies, it was found that vitamin E has antioxidant, anti-inflammatory, anticoagulant, and antifibroblastic effects to a similar effect of Lycopene. Yetkin et al. demonstrated that intraperitoneal vitamin E injection and human amniotic membrane separately reduced post-operative adhesion in rats; however, a synergistic increase in their effects could not be demonstrated with their co-administration.[33] The results of our study are consistent with these studies.

Our study had some limitations. First, it was the route of application of the anti-adhesion agent. We chose this method in our study because the intraperitoneal route is generally used in the literature. Another limitation is that the dose of intraperitoneal lycopene required to prevent adhesion is unknown. In this study, we used the doses used in animal models of oxidative stress.

Conclusions

Histological and mechanical parameters obtained in our study suggest that lycopene, which we use as an anti-adhesion agent, is effective in preventing intra-abdominal adhesions and does not negatively affect wound healing.

Funding

The authors declare that they have not received funding.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki.

Confidentiality, informed consent, and ethical approval. The study does not involve patient personal data. The SAGER guidelines were followed according to the nature of the study. This study was approved by our University Animal Experiments Local Ethics Committee (April 26, 2017, Protocol No: 2017/011).

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

References

1. Diamond MP. Incidence of Postsurgical Adhesions. Peritoneal Surgeryed. Berlin: Springer; 2000. p. 217-20.
2. Mavigök E, Bakacak M, Yazar FM, Bakacak Z, Yaylalı A, Boran ÖF, et al. A comparison in an experimental rat model of the effects on adhesion formation of different hemostatic methods used in abdominopelvic surgery. Ginekol Pol. 2019;90:507-12.
3. Schreinemacher MH, Richard P, Bakkum EA, Van Goor H, Bouvy ND. Adhesion awareness: a national survey of surgeons. World J Surg. 2010; 34:2805-12.
4. Risberg B. Adhesions: preventive strategies. Eur J Surg Suppl. 1997; 577:32-9.
5. Yue YS, Song X, Ma C, Li D, Hu X, Chen F, et al. Lycopene ameliorated DSS-ınduced colitis by improving epithelial barrier functions and ınhibiting the *Escherichia coli* adhesion in mice. J Agric Food Chem. 2024; 72:5784-96.
6. Yang PM, Chen HZ, Huang YT, Hsieh CW, Wung BS. Lycopene inhibits NF-κB activation and adhesion molecule expression through Nrf2-mediated heme oxygenase-1 in endothelial cells. Int J Mol Med. 2017;39:1533-450.
7. Zamani M, Behmanesh Nia F, Ghaedi K, Mohammadpour S, Amirani N, Goudarzi K, et al. The effects of lycopene and tomato consumption on cardiovascular risk factors in adults: a grade assessment systematic review and meta-analysis. Curr Pharm Des. 2023;29:1671-700.
8. Long Y, Paengkoum S, Lu S, Niu X, Thongpea S, Taethaisong N, et al. Physicochemical properties, mechanism of action of lycopene and its application in poultry and ruminant production. Front Vet Sci. 2024; 11:1364589.
9. Gao X, Lin B, Chen C, Fang Z, Yang J, Wu S, et al. Lycopene from tomatoes and tomato products exerts renoprotective effects by ameliorating oxidative stress, apoptosis, pyroptosis, fibrosis, and inflammatory injury in calcium oxalate nephrolithiasis: the underlying mechanisms. Food Funct. 2024;15:4021-36.
10. Salunke MR, Kala K, Mandlik DS, Ganeshpurkar A, Kulkarni R, Shinde V. Lycopene potentiates wound healing in streptozotocin-induced diabetic rats. J Diabetes Metab Disord. 2024;23:1359-70.
11. Farjah GH, Mohammdzadeh S, Zirak Javanmard M. The effect of lycopene in egg shell membrane guidance channel on sciatic nerve regeneration in rats. Iran J Basic Med Sci. 2020;23:527-33.
12. Zhang X, Zhou Q, Qi Y, Chen X, Deng J, Zhang Y, et al. The effect of tomato and lycopene on clinical characteristics and molecular markers of UV-induced skin deterioration: a systematic review and meta-analysis of intervention trials. Crit Rev Food Sci Nutr. 2024;64:6198-217.
13. Shih CM, Hsieh CK, Huang CY, Huang CY, Wang KH, Fong TH, et al. Lycopene inhibit IMQ-induced psoriasis-like inflammation by inhibiting ICAM-1 production in mice. Polymers (Basel). 2020;12:1521.
14. Shafe MO, Gumede NM, Nyakudya TT, Chivandi E. Lycopene: a potent antioxidant with multiple health benefits. J Nutr Metab. 2024;2024: 6252426.
15. Kulhan NG, Kulhan M, Turkler C, Ata N, Kiremitli T, Kiremitli S, et al. Effect of lycopene on oxidative ovary-damage induced by cisplatin in rats. Gen Physiol Biophys. 2019;38:253-8.
16. Burgess LC, Rice E, Fischer T, Seekins JR, Burgess TP, Sticka SJ, et al. Lycopene has limited effect on cell proliferation in only two of seven human cell lines (both cancerous and noncancerous) in an *in vitro* system with doses across the physiological range. Toxicol *In Vitro*. 2008;22:1297-300.
17. Güney G, Kaya C, Oto G, Yıldırım S, Özdemir H, Tokmak A. Effects of quercetin and surgicel for preventing adhesions after gynecological surgery: a rat uterine horn model. J Obstet Gynaecol Res. 2017;43:179-84.
18. Leach RE, Burns JW, Dawe EJ, SmithBarbour MD, Diamond MP. Reduction of postsurgical adhesion formation in the rabbit uterine horn model with use of hyaluronate/carboxymethylcellulose gel. Fertil Steril 1998; 69: 415-418.
19. Hooker GD, Taylor BM, Driman DK. Prevention of adhesion formation with use of sodium hyaluronate-based bioresorbable membrane in a rat model of ventral hernia repair with polypropylene mesh--a randomized, controlled study. Surgery. 1999;125:211-6.
20. Çakalağaoğlu F. Tissue processing-Doku takibi. J Aegean Pathol. 2005;2:29-34.
21. Ekicioğlu G, Özkan N, Şalvaazar E. Hematoksilen-eozin (hematoxylin-eosin)(H&E). Aegean Pathol J. 2005;2:58-61.
22. Goldstein M, Watkins S. Immunohistochemistry. Curr Protoc Mol Biol. 2008;81:14.6.1-23.
23. Mihara M, Uchiyama M. Determination of malonaldehyde precursor in tissues by thiobarbituric acid test. Anal Biochem. 1978;86:271-8.
24. Erel O. A novel automated direct measurement method for total antioxidant capacity using a new generation, more stable ABTS radical cation. Clin Biochem. 2004;37:277-85.
25. Moris D, Chakedis J, Rahnemai-Azar AA, Wilson A, Hennessy MM, Athanasiou A, et al. Postoperative abdominal adhesions: clinical significance and advances in prevention and management. J Gastrointest Surg. 2017;21:1713-22.
26. Portz D, Elkins T, White R, Warren J, Adadevoh S, Randolph J. Oxygen free radicals and pelvic adhesion formation: I. Blocking oxygen free radical toxicity to prevent adhesion formation in an endometriosis model. Int J Fertil. 1991;36:39-42.
27. Başbuğ M, Aygen E, Tayyar M, Kaya E, Narin F, Oktem O. Hyaluronic acid plus heparin for improved efficacy in prevention of adhesion formation in rat uterine horn model. Eur J Obstet Gynecol Reprod Biol. 1998; 78:109-12.
28. Farhangi MA, Tajmiri S. The effects of powdered black cumin seeds on markers of oxidative stress, intracellular adhesion molecule (ICAM)-1 and vascular cell adhesion molecule (VCAM)-1 in patients with Hashimoto's thyroiditis. Clin Nutr ESPEN. 2020;37:207-12.
29. Marino M, Del Bo C, Tucci M, Klimis-Zacas D, Riso P, Porrini M. Modulation of adhesion process, e-selectin and VEGF production by anthocyanins and their metabolites in an *in vitro* model of atherosclerosis. Nutrients. 2020;12:655.
30. Roohbakhsh Y, Rahimi VB, Silakhori S, Rajabi H, Rahmanian-Devin P, Samzadeh-Kermani A, et al. Evaluation of the effects of peritoneal lavage with rosmarinus officinalis extract against the prevention of postsurgical-ınduced peritoneal adhesion. Planta Med. 2020;86:405-14.
31. Linsky CB , Diamond MP, Cunningham T , Constantine B, DeCherney AH, diZerega GS. Adhesion reduction in the rabbit uterine horn model using an absorbable barrier, TC-7. The Journal of Reproductive Medicine. 1987;32(1):17-20.
32. Fletcher NM, Awonuga AO, Saed MG, Abu-Soud HM, Diamond MP, Saed GM. Lycopene, a powerful antioxidant, significantly reduces the development of the adhesion phenotype. Syst Biol Reprod Med. 2014; 60:14-20.
33. Yetkin G, Uludag M, Citgez B, Karakoc S, Polat N, Kabukcuoglu F. Prevention of peritoneal adhesions by intraperitoneal administration of vitamin E and human amniotic membrane. Int J Surg. 2009;7:561-5.