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Original Article

Preventive Effect of Enalapril and Ellagic Acid on Postsurgical Abdominal Adhesions in Rat Models

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Abstract

Introduction: Abdominal adhesions are postoperative consequences that predispose patients to complications. Due to the anti-inflammatory and antifibrotic effects of enalapril (EPR) and ellagic acid (EA), this study aimed to determine their therapeutic potential in reducing abdominal adhesions after surgery.

Methods: Rats were divided into negative control, sham, positive control, EA 8 mg/kg i.p.), and combined intervention (EA 8 mg/kg and EPR 5 mg/kg, i.p.) groups. After 7 days of treatment, adhesion band formation and tissue histopathology were evaluated, followed by measuring malondialdehyde (MDA), total antioxidant capacity (TAC), and the expression of interleukin-6 (IL-6), plasminogen activator inhibitor (PAI)-1, collagen 1, and collagen 3. Statistical analyses were performed using GraphPad prism 9.

Results: Treatment with EA alone and in combination with EPR significantly reduced adhesion formation compared with the positive control ($P<0.01$ and $P<0.001$, respectively). The positive control group exhibited increased oxidative stress, characterized by higher MDA levels and lower TAC. However, combined EA and EPR substantially decreased MDA while increasing TAC (both $P<0.05$). Additionally, adhesion induction markedly increased *IL-6*, *PAI-1*, *collagen 1*, and *collagen 3* gene expression. EA alone and in combination with EPR noticeably downregulated IL-6, PAI-1, and collagen 1 expression compared with the positive control ($P<0.001$).

Conclusion: EPR and EA potentiated the anti-inflammatory, antioxidant, and antifibrotic properties of each other. Nonetheless, more studies are needed to prove the therapeutic effect of this combination on postsurgical abdominal adhesion.

Keywords: Ellagic acid, Enalapril, Surgical adhesion, Abdominal surgery

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Introduction

Postoperative adhesion is a fibrotic bond between two organ surfaces inside body cavities that is created by fibrinolysis imbalance and cellular secretion, followed by surgical area injury. It fluctuates from a slight layer of connective tissue to a thick fibrotic bond containing blood vessels and nervous tissue (1). Moreover, postoperative adhesion is a common clinical complication and has high morbidity and mortality. Furthermore, this complication leads to an increase in the length of hospital stay and healthcare costs (2). Nonetheless, the mechanism of adhesion formation is not yet clear, and some research suggests that it has a multifactorial etiology. However, existing studies indicate that it is a tissue regeneration process associated with inflammatory responses, trauma-induced tissue damage, and immune and cellular responses (3). Although surgical techniques have improved, abdominal adhesions mostly form after abdominal surgical interventions, and they are an unavoidable consequence of abdominal surgery (4). They face challenges such as the risk of disease recurrence and the inherent risks associated with treatment methods, necessitating a review of how these treatments are managed (5,6). Therefore, there is a pressing need to explore and develop innovative therapeutic strategies for managing abdominal-pelvic adhesions.

One approach to prevent abdominal adhesions after surgery is to use anti-inflammatory and anti-fibrinolytic drugs (4,7). Enalapril (EPR) is an angiotensin-converting enzyme (ACE) inhibitor and decreases blood pressure (8). Many studies have been conducted on the antifibrotic and anti-inflammatory effects of EPR. Previous studies have demonstrated that ACE inhibitors enhance the expression of antifibrotic biomarkers (9-11). In addition, ellagic acid (EA) is a natural polyphenol that has anti-hepatotoxic and anti-cancer antioxidant properties and is found in many fruits. According to some studies, EA has antifibrotic properties in hypertrophic scar fibroblasts (12), cardiac fibrosis (13), and intrauterine adhesions (14). The effectiveness and safety of EA and EPR in reducing abdominal adhesions after surgery have not been evaluated so far. Thus, this study seeks to investigate the preventive effect of EPR and EA on postsurgical abdominal adhesions in a rat model.

Materials and Methods

Study Design

A randomized, controlled, parallel-group, five-arm preclinical animal experiment was conducted using a rat

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model of postsurgical abdominal adhesions.

Animals and Experimental Groups

Forty male Wistar rats were randomly allocated to five parallel experimental groups (n = 8 per group) using a computer-generated randomization sequence (15); the negative control group underwent no induction of postsurgical adhesion and treatment, and the sham group underwent surgery without induction of postsurgical adhesion. Further, the positive control group underwent induction of postsurgical adhesion without treatment, and the EA group underwent induction of postsurgical adhesion and EA treatment, and the EA plus EPR group underwent induction of postsurgical adhesion and EA + EPR treatment. The study employed a controlled experimental design to evaluate the preventive effects of EA alone and in combination with EPR on postsurgical abdominal adhesion formation. Furthermore, the adhesion model was induced by laparotomy followed by standardized abrasion of the cecal and abdominal wall surfaces. Moreover, treatment groups received intraperitoneal EA (8 mg/kg) alone (16,17) or in combination with EPR (5 mg/kg) (18) for seven consecutive days. Subsequently, macroscopic adhesion severity, histopathological changes, oxidative stress (OS) markers, and the expression of inflammatory and fibrotic genes were assessed. It should be noted that investigators responsible for macroscopic adhesion scoring and histopathological evaluation were blinded to group allocation.

Forty male Wistar rats, approximately 3–4 months of age and weighing 200–250 g, were obtained from the Pasteur Institute of Iran. The animals were housed under standard laboratory conditions in an animal facility maintained on a 12-hour light/12-hour dark cycle at 22 ± 1°C. Food and water were provided ad libitum throughout the experimental period.

Blinding Method

The investigator assessing adhesion scores and the pathologist evaluating histological sections were blinded to group allocation.

Postoperative Adhesion Band Models

Anesthesia was induced with an intraperitoneal injection of ketamine 60 mg/kg and xylazine 10 mg/kg (19). Next, the peritoneal cavity was opened by a 1.5 cm incision on the abdominal midline. Then, the surface of the cecum and abdominal wall was briefly scratched with a sterile rough surface (proline mesh) to generate partial petechial hemorrhages; the abdominal muscle layer was sutured with absorbable suture, and the skin layer was sutured with nylon thread to form adhesion bands (20).

Evaluation of Adhesion Scores

Adhesion degree in macroscopic examination was calculated based on the Ahmet-Canbaz scale: **0:** no adhesion, **I:** presence of a narrow adhesive band without blood vessels and easily separated, **II:** presence of 2 narrow adhesive bands without blood vessels and easily separated, **III:** the presence of 3 narrow, avascular, easily separable adhesive bands, and **IV:** the presence of more than 3 nonvascular, easily separable adhesive bands, or scattered and diffuse adhesions (20).

Histological Staining

Upon completion of the experimental procedures, the animals were anesthetized and euthanized, after which the required tissue specimens were harvested. Samples designated for molecular or biochemical analyses were immediately snap-frozen in liquid nitrogen, whereas those intended for histological evaluation were fixed in 10% formalin for 48 hours and subsequently subjected to routine tissue processing and paraffin embedding. Next, sections with a thickness of 5 μm were prepared from the paraffin-embedded tissues and stained with hematoxylin and eosin. The stained sections were microscopically examined by a qualified pathologist for histopathological assessment. Afterward, adhesion degree was assessed based on the severity of fibrosis (0: no fibrosis, I: low, II: moderate, and III: high), and the inflammation degree was measured based on predefined histological scoring system (0: no inflammation, I: giant cells, lymphocytes, and plasma cells, II: giant cells, plasma cells, eosinophils, and neutrophils, and III: infiltration of inflammatory cells and microabscesses) (20).

Oxidative Stress Markers Analysis

Total antioxidant capacity (TAC) was assessed in the tissue samples using the ferric-reducing antioxidant power assay. The assay was performed according to a previously described protocol under acidic conditions (pH: 3.6) at 37°C. The absorbance of each sample was determined following a 30-minute incubation period. TAC was expressed as mmol Fe^{2+}/mg total protein, representing the overall ferric-reducing antioxidant capacity of the protein-associated antioxidants present in the samples (21).

Additionally, malondialdehyde (MDA) levels in the tissue samples were estimated using a previously established method. Briefly, MDA was quantified based on its reaction with thiobarbituric acid, resulting in the formation of a colored complex. The absorbance of the reaction products was subsequently measured at 562 nm using a microplate enzyme-linked immunosorbent assay reader (22).

Gene Expression Analysis

Gene expression levels in the tissue samples were determined by quantitative real-time polymerase chain reaction. Briefly, the collected tissues were homogenized in TRIzol reagent (Invitrogen), followed by extraction of total ribonucleic acid according to the manufacturer's protocol. For reverse transcription, 1 μg of purified ribonucleic acid was converted into complementary DNA using the PrimeScript RT reagent kit, followed by quantifying the expression levels of interleukin-6 (IL-6), plasminogen activator inhibitor (PAI)-1, collagen 1, and collagen 3 using SYBR Premix Ex Taq chemistry on a LightCycler

real-time polymerase chain reaction system. Each reaction was performed in triplicate, and the experiment was independently repeated twice. In addition, beta-2-microglobulin was used as the endogenous reference gene for normalization. Furthermore, relative changes in the expression of the target genes were calculated using the $2^{-\Delta\Delta Ct}$ relative expression method (23,24). Primer sequences are provided in Table 1.

Statistical Analysis

Statistical analyses were performed using GraphPad Prism software version 9. The normal distribution of data was checked by the Kolmogorov-Smirnov test. Further, differences among experimental groups were analyzed using one-way analysis of variance (ANOVA), followed by Tukey's multiple-comparisons test. Data are presented as the mean ± standard error of the mean (SEM). Finally, data normality was assessed using the Shapiro-Wilk test, and homogeneity of variances was evaluated before analysis. A probability value of $P < 0.05$ indicated statistical significance.

Results

Enalapril and Ellagic Acid Antifibrotic Properties and Reduced Postsurgical Abdominal Adhesions

The effects of EA and EPR on the process of fibrosis and the formation of adhesions were evaluated in this study (Figure 1). One-way ANOVA followed by Tukey's post-hoc test showed that adhesion intensity in the positive control group was significantly higher than that in the negative control group ($P < 0.001$). Likewise, EA and EA with EPR administration markedly reduced adhesion intensity compared with the positive control group ($P < 0.01$ and $P < 0.001$, respectively).

Histopathological evaluation revealed that EA and EPR decreased inflammation, fibrinolysis, and adhesion at the surgical site compared with the positive control group (Figure 2).

Enalapril and Ellagic Acid Decreased the Malondialdehyde Levels

To assess the antioxidant effects of EA and EPR, MDA levels were measured as an indicator of OS. Based on the results (Figure 3), the positive control group exhibited a significant elevation in MDA levels compared with the negative control group ($P < 0.001$). Treatment with EA in combination with EPR significantly reduced MDA levels relative to the positive control group ($P < 0.05$).

Enalapril and Ellagic Acid Increased Total Antioxidant Capacity

The results (Figure 4) demonstrated that TAC was substantially lower in the positive control group than in the negative control group ($P < 0.05$). Conversely, EA combined with EPR markedly increased TAC levels compared with the positive control group ($P < 0.05$).

Enalapril and Ellagic Acid Downregulation of IL-6, PAI-1, Collagen 1, and Collagen 3 Gene Expression

The expression of *IL-6*, *PAI-1*, and *collagen 1* and *collagen 3* genes was investigated, and the results (Figure 5A-D) showed that *IL-6* ($P < 0.001$), *PAI-1* ($P < 0.01$), and *collagen 1* ($P < 0.05$) and *collagen 3* ($P < 0.001$) gene expression was significantly increased in the positive control group compared with the negative control group. On the other hand, EA alone and EA combined with EPR remarkably decreased *IL-6*, *PAI-1*, and *collagen 1* gene expression compared with the positive control group ($P < 0.001$).

Discussion

This study evaluated the preventive effect of EPR and EA on postsurgical abdominal adhesions in a rat model. The results confirmed that administration of EA alone and the EA and EPR combination substantially decreased postoperative adhesion band formation in rat models. Further, EA and the EA-EPR combination reduced the

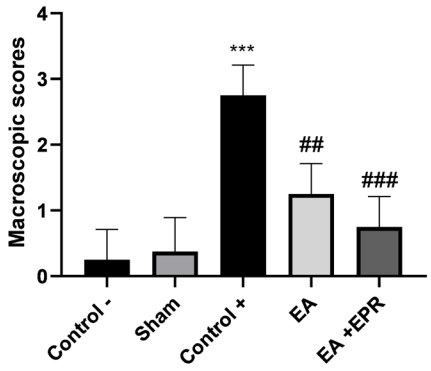

Figure 1. Effects of Enalapril and Ellagic Acid on Fibrosis and Postoperative Abdominal Adhesion Formation. *Note*. EA: Ellagic acid; EPR: Enalapril; ANOVA: Analysis of variance; SEM: Standard error of the mean; Data are presented as means ± SEM. Statistical comparisons were performed using one-way ANOVA followed by Tukey's multiple-comparisons post-hoc test. Each experimental group consisted of eight animals (n = 8). $^{***}P < 0.001$ versus the saline-treated control group; $^{\#\#\#}P < 0.001$ versus the positive control group

Table 1. Primer Sequences

Primer	Forward Sequence	Reverse Sequence
PAI-1	GGAGAAGCTGGGCATGACTG	CACTGTGCCGCTCTCGTTCA
Collagen-1	GCGAAGGCAACAGTCGATTC	CCCAAGTTCCGGTGTGACTC
Collagen-3	CAGCTGGCCTTCCTCAGACTT	GCTGTTTTTGCAGTGGTATGTAATG
β-actin	GTCTTCCCCTCCATCGTG	TGCTTGCTGATCCACATCTG
IL-6	GACTTCTCCCCCACCGTATC	TCCTCACAGCCCCTTCTTTC

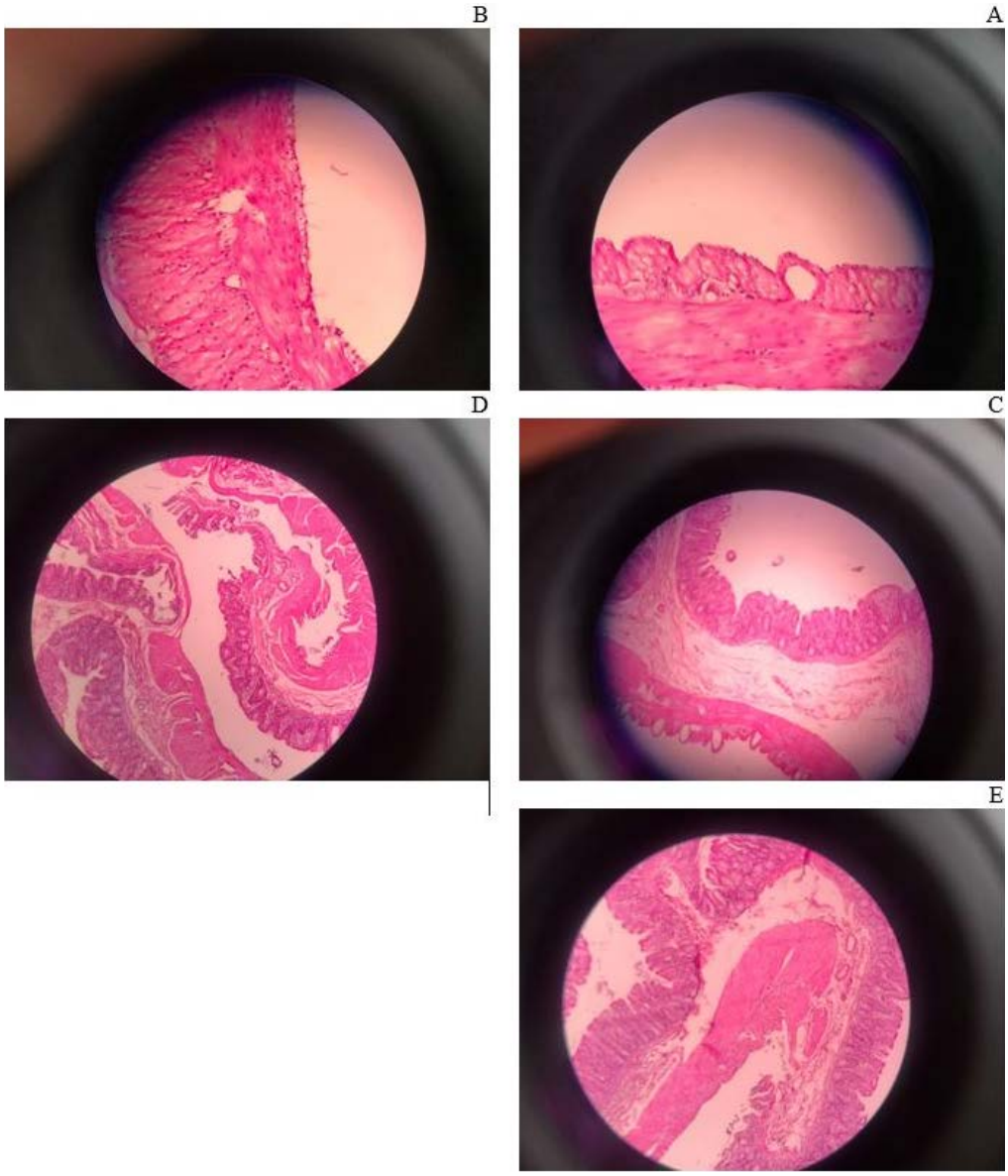

Figure 2. Histopathological Evaluation of Adhesion in the Studied Groups: Negative Control Group **(A)**, Positive Control Group **(B)**, Sham Group **(C)**, Ellagic Acid Group **(D)**, and Ellagic Acid + Enalapril Group **(E)**. *Note*. Images with hematoxylin and eosin staining and light microscope

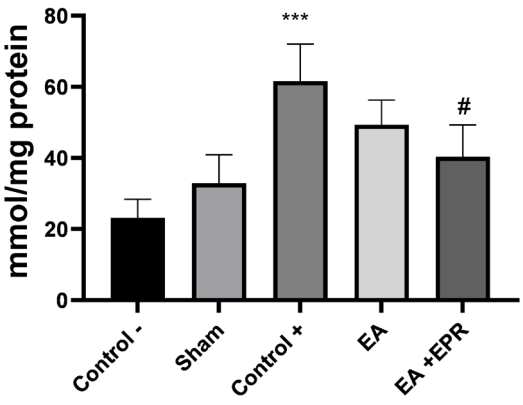

Figure 3. Effects of Enalapril and Ellagic Acid on MDA Levels. *Note*. EA: Ellagic acid; EPR: Enalapril; MDA: Malondialdehyde; SEM: Standard error of the mean; ANOVA: Analysis of variance; Data, expressed as means ± SEM, were analyzed using one-way ANOVA followed by Tukey's multiple-comparisons post-hoc test. Each group included eight animals (n = 8). $^{***}P < 0.001$ versus the saline-treated control group; $^{*}P < 0.05$ versus the positive control group

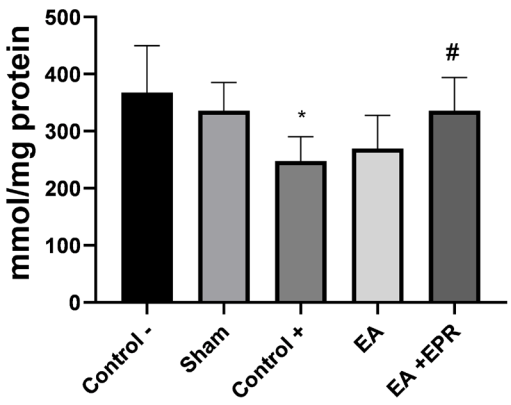

Figure 4. Effects of Enalapril and Ellagic Acid on TAC. *Note*. EA: Ellagic acid; EPR: Enalapril; TAC: Total antioxidant capacity; SEM: Standard error of the mean; ANOVA: Analysis of variance; Data provided as means ± SEM were analyzed using one-way ANOVA followed by Tukey's multiple-comparisons post hoc test. Each group contained eight animals (n = 8). $^{*}P < 0.05$ versus the saline-treated control group; $^{\#}P < 0.05$ versus the positive control group

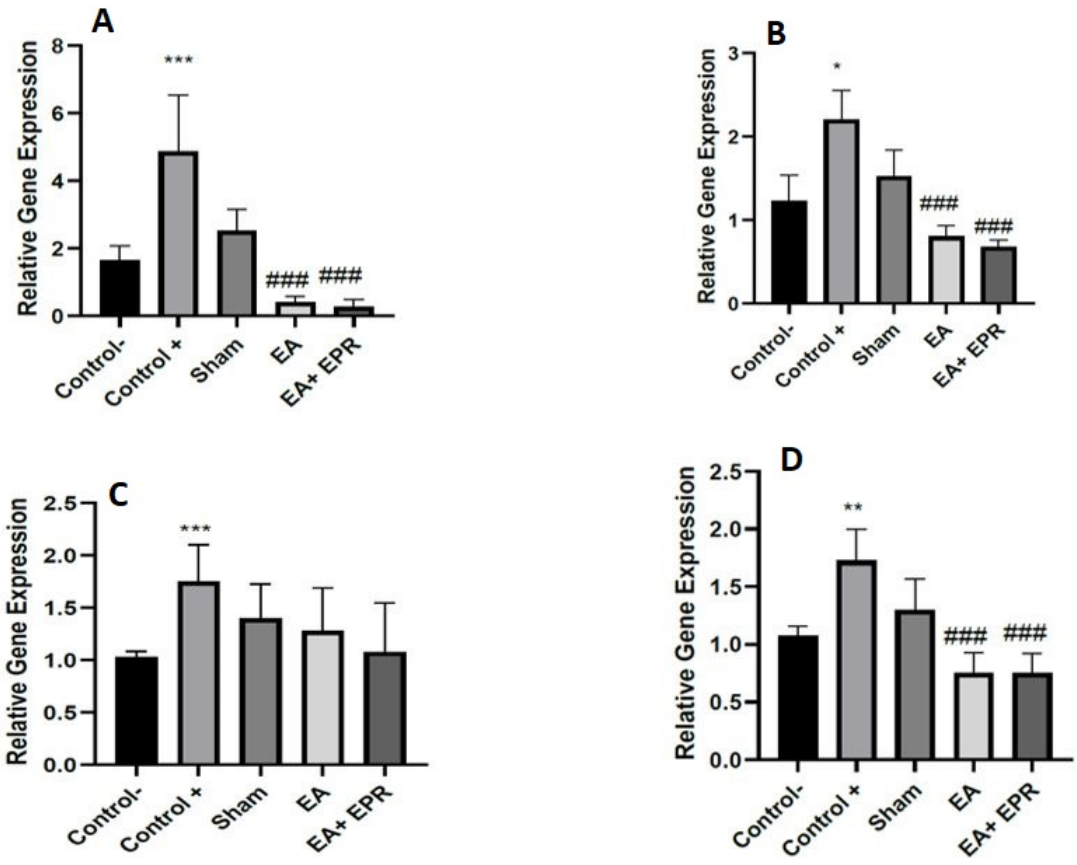

Figure 5. Effects of Enalapril and Ellagic Acid on the Expression of *IL-6* **(A)**, *Col1* **(B)**, *Col3* **(C)**, and *PAI-1* **(D)** Genes. *Note*. EA: Ellagic acid; EPR: Enalapril; SEM: Standard error of the mean; ANOVA: Analysis of variance Data demonstrated as means ± SEM were analyzed using one-way ANOVA followed by Tukey's multiple-comparisons post hoc test. Each group encompassed eight animals (n = 8). $^{*}P<0.05$, $^{**}P<0.01$, and $^{***}P<0.001$ versus the saline-treated control group; $^{\#\#\#}P<0.001$ versus the positive control group

inflammatory reaction related to adhesion by decreasing inflammatory cell infiltration. Based on the findings, EPR strengthened the anti-inflammatory and antifibrotic properties of EA, indicating the potent anti-adhesive activity of the EA-EPR combination. Previous animal studies have shown the protective effects of EA against peritoneal adhesions due to its anti-inflammatory, antioxidant, and anti-angiogenic effects (15,25), which conforms to our findings. Likewise, EPR, an ACE inhibitor, demonstrates anti-adhesion effects; some studies report that it reduces postoperative intra-abdominal adhesions by targeting OS and inflammation pathways (26,27). Renin-angiotensin-aldosterone inhibitors play a role in the fibrinolysis process by targeting this system (27). The findings of the above studies on the anti-adhesion and anti-pyrosis effects of EPR and EA corroborate our findings, although our study investigated and confirmed the combined effect of the two agents for the first time.

In addition to the observation of adhesion bands, fibrosis, and inflammation in histopathological examination, an increase in MDA level and a decrease in TAC as a marker of OS, as well as an increase in the expression of *IL-6*, *collagen 1*, and *collagen 3*, and *PAI-1* genes, were observed in the positive control group's tissue, revealing the pathological adhesion bond process. Immediately after peritoneal injury, damaged cells produce inflammatory cytokines that stimulate the healing process through the formation of premature adhesions from fibrin deposits (28). In this regard, studies confirm that inflammation and OS contribute to postsurgical adhesion formation and affect fibrinolysis and adhesion band formation (29,30). Similarly, Ghadiri et al concluded that adhesion band formation is associated with increased MDA levels and OS (31). Furthermore, Özler et als indicated that IL-6 and PAI play a role in the occurrence of post-laparotomy peritoneal adhesions (32).

Additionally, our results showed that EA alone did not significantly change MDA and TAC levels. Further, Shahidi et al found that EA (25 mg/kg) did not substantially change MDA and TAC levels, whereas EA (50 mg/kg) increased TAC and decreased MDA in diabetic rats (33). In contrast, Mirzaie et al observed that EA (180 mg of ellagic acid per day) markedly decreased MDA and increased TAC in irritable bowel syndrome patients (34). These contradictions are probably due to differences in study protocols, dose, and treatment duration. Although EA alone did not cause a significant change in MDA and TAC levels, its combination with EPR caused a considerable decrease in MDA and a noticeable increase in TAC. In this regard, some previous studies have shown the antioxidant and anti-inflammatory effects of EPR in reducing the oxidation of proteins and lipids (e.g., MDA) and increasing TAC (35,36). These findings highlight to the anti-inflammatory and antioxidant synergistic

effects of EA and EPR. Therefore, EPR strengthens the anti-inflammatory and antioxidant effects of EA, and the combination of these two substances reduces inflammation and regulates the OS imbalance in the operation area.

Moreover, our results demonstrated that EA and EPR downregulated the expression of inflammation-related, OS-related, and fibrinolysis-related genes, including *IL-6*, *collagen 1* and *collagen 3*, and *PAI-1*. This is supported by the findings of Mannino et al, showing that EA reduced pro-fibrotic protein expression and intracellular reactive oxygen species accumulation, including IL-6, tumor necrosis factor-alpha, and transforming growth factor-β1-SMAD family member 2/SMAD family member 3- matrix metalloproteinase-2/matrix metalloproteinase-9 (13). In addition, Ghosh et al concluded that EPR (10 mg/kg) has a protective effect against kidney fibrosis and inflammation by reducing plasma concentration and the expression of *TNF-α* and *β1IL* genes (37). Similar to our study, Walter et al reported that EPR reduces PAI-1 levels in myocardial infarction patients (38). The results of the present study are consistent with those of the above-mentioned studies, indicating the mechanism of adjustment of *IL-6*, *collagen*, and *PAI-1* gene expression in the anti-adhesive activity of EA and EPR.

Conclusion

The findings revealed that combined EA and EPR treatment was associated with reduced adhesion formation and favorable changes in selected inflammatory, OS, and fibrosis-related outcomes in this rat model. Additionally, the anti-inflammatory and antioxidant effects of EA within the surgical site could contribute to its antifibrotic properties. Ultimately, the novelty of the present work is the protective effect of the EA and EPR combination against postsurgical adhesion in an animal study.

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Artificial Intelligence Use Disclosure

During the preparation of this manuscript, the authors used Grammarly and ChatGPT for language and grammar editing. All content generated with the assistance of this tool was carefully reviewed, validated, and revised by the authors in order to ensure accuracy, originality, and scholarly rigor. The authors assume full responsibility for the integrity and final content of the published articles.

Authors' Contribution

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Writing–Original Draft: Nader Mohseni, Iraj Baratpour, Borzoo Khaledifar
Writing–Review & Editing: Nader Mohseni, Iraj Baratpour, Borzoo Khaledifar

Competing Interests

The authors have no conflict of interests to declare.

Ethical Approval

This study was approved by the Institutional Animal Ethics Committee for animal investigation of Shahrekord University of Medical Sciences (ethical code IR.SKUMS.REC.1400.085). The ARRIVE guidelines were also utilized for reporting experiments involving live animals, thereby promoting ethical research practices. Moreover, the reported experiments followed the standards outlined in the US National Research Council's "Guide for the Care and Use of Laboratory Animals." Furthermore, all procedures were approved by the Institutional Animal Care and Use Committee, ensuring compliance with ethical guidelines and efforts to minimize animal suffering.

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References

1. Morris RJ 3rd, Nori T, Sandler AD, Kofinas P. Postoperative Adhesions: Current Research on Mechanisms, Therapeutics and Preventative Measures. Biomed Mater Devices 2025;3(2):897-937. doi:10.1007/s44174-024-00236-7
2. Kitundu JH, Mashauri HL. Clinical Implications of Postsurgical Adhesions and Fibrosis: The Role of Vitamin C in Prevention and Control. Health Sci Rep 2025;8(2): e70393. doi:10.1002/hsr2.70393
3. Fatehi Hassanabad A, Zarzycki AN, Jeon K, Deniset JF, Fedak PWM. Post-Operative Adhesions: A Comprehensive Review of Mechanisms. Biomedicines 2021;9(8):867. doi:10.3390/biomedicines9080867
4. Marietta M, Desai H. Open Inguinal Hernia Repair. [Updated 2026 Aug 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan. Available from:https://www.ncbi.nlm.nih.gov/sites/books/NBK459309/.
5. Shen CJ, Wang JJ. Advancements in the clinical management of adhesive small bowel obstruction: A perspective. Medicine (Baltimore) 2025;104(27): e43246. doi:10.1097/md.0000000000043246
6. Di Saverio S, Coccolini F, Galati M, Smerieri N, Biffl WL, Ansaloni L, et al. Bologna guidelines for diagnosis and management of adhesive small bowel obstruction (ASBO): 2013 update of the evidence-based guidelines from the world society of emergency surgery ASBO working group. World J Emerg Surg 2013;8(1):42. doi:10.1186/1749-7922-8-42
7. Nakashima M, Takeuchi M, Kawakami K. Effectiveness of barrier agents for preventing postoperative bowel obstruction after laparoscopic surgery: a retrospective cohort study. Surg Today 2021;51(8):1335-42. doi:10.1007/s00595-021-02258-w
8. Olanrewaju OA, Saleem A, Ansah Owusu F, Pavani P, Ram R, Varrassi G. Contemporary Approaches to Hernia Repair: A Narrative Review in General Surgery. Cureus 2023;15(12): e51421. doi:10.7759/cureus.51421
9. Sanie-Jahromi F, Khademi B, Owji N. Effect of enalapril and losartan on the expression of genes involved in inflammation, fibrogenesis, and apoptosis in orbital fibroblasts of graves' ophthalmopathy. BMC Res Notes 2025;18(1):454. doi:10.1186/s13104-025-07419-5
10. Khan YH, Qasim S, Uttra AM, Alotaibi NH, Alanazi AS, Alzarea AI, Alatawi AD, Hussain Mallhi T. Enalapril attenuated CFA provoked arthritic manifestation by modulating proinflammatory and anti-inflammatory cytokine network. Life Sci. 2023 Jul 1;324:121742. doi: 10.1016/j.lfs.2023.121742

11. Ghazi-Khansari M, Mohammadi-Karakani A, Sotoudeh M, Mokhtary P, Pour-Esmaeil E, Maghsoud S. Antifibrotic effect of captopril and enalapril on paraquat-induced lung fibrosis in rats. J Appl Toxicol 2007;27(4):342-9. doi:10.1002/jat.1212
12. Liu X, Gao X, Li H, Li Z, Wang X, Zhang L, et al. Ellagic acid exerts anti-fibrotic effects on hypertrophic scar fibroblasts via inhibition of TGF-β1/Smad2/3 pathway. Appl Biol Chem 2021;64(1):67. doi:10.1186/s13765-021-00641-2
13. Mannino F, Imbesi C, Bitto A, Minutoli L, Squadrito F, D'Angelo T, et al. Anti-oxidant and anti-inflammatory effects of ellagic and punicic acid in an in vitro model of cardiac fibrosis. Biomed Pharmacother 2023;162:114666. doi:10.1016/j.biopha.2023.114666
14. Saribas GS, Akarca Dizakar O, Ozogul C, Celik E, Ergoren MC. Ellagic acid increases implantation rates with its antifibrotic effect in the rat model of intrauterine adhesion. Pathol Res Pract 2023;246:154499. doi:10.1016/j.prp.2023.154499
15. Allahverdi TD, Allahverdi E, Yayla S, Deprem T, Merhan O, Vural S. The comparison of the effects of ellagic acid and diclofenac sodium on intra-abdominal adhesion: an in vivo study in the rat model. Int Surg 2014;99(5):543-50. doi:10.9738/intsurg-d-14-00065.1
16. Mansouri MT, Hemmati AA, Naghizadeh B, Mard SA, Rezaie A, Ghorbanzadeh B. A study of the mechanisms underlying the anti-inflammatory effect of ellagic acid in carrageenan-induced paw edema in rats. Indian J Pharmacol 2015;47(3):292-8. doi:10.4103/0253-7613.157127
17. Kannan MM, Quine SD. Ellagic acid inhibits cardiac arrhythmias, hypertrophy and hyperlipidaemia during myocardial infarction in rats. Metabolism 2013;62(1):52-61. doi:10.1016/j.metabol.2012.06.003
18. Cozzoli A, Nico B, Sblendorio VT, Capogrosso RF, Dinardo MM, Longo V, et al. Enalapril treatment discloses an early role of angiotensin II in inflammation- and oxidative stress-related muscle damage in dystrophic mdx mice. Pharmacol Res 2011;64(5):482-92. doi:10.1016/j.phrs.2011.06.002
19. Mechelinck M, Kupp C, Krüger JC, Habigt MA, Helmedag MJ, Tolba RH, et al. Oxygen inhalation improves postoperative survival in ketamine-xylazine anaesthetised rats: An observational study. PLoS One 2019;14(12): e0226430. doi:10.1371/journal.pone.0226430
20. Parsaei P, Karimi M, Asadi SY, Rafieian-Kopaei M. Bioactive components and preventive effect of green tea (Camellia sinensis) extract on post-laparotomy intra-abdominal adhesion in rats. Int J Surg 2013;11(9):811-5. doi:10.1016/j.ijsu.2013.08.014
21. Aldarmaa J, Liu Z, Long J, Mo X, Ma J, Liu J. Anti-convulsant effect and mechanism of Astragalus mongholicus extract in vitro and in vivo: protection against oxidative damage and mitochondrial dysfunction. Neurochem Res 2010;35(1):33-41. doi:10.1007/s11064-009-0027-4
22. Nasiri-Boroujeni S, Rahimi-Madiseh M, Lorigooini Z, Piroti K, Rafieian-Koupaei M, Amini-Khoei H. NMDA Receptor Mediates the Anticonvulsant Effect of Hydroalcoholic Extract of *Artemisia persica* in PTZ-Induced Seizure in Mice. Evid Based Complement Alternat Med 2021;2021:6422451. doi:10.1155/2021/6422451
23. Haj-Mirzaian A, Amiri S, Amini-Khoei H, Rahimi-Balaei M, Kordjazy N, Olson CO, et al. Attenuation of oxidative and nitrosative stress in cortical area associates with antidepressant-like effects of tropisetron in male mice following social isolation stress. Brain Res Bull 2016;124:150-63. doi:10.1016/j.brainresbull.2016.04.018
24. Rahimi-Madiseh M, Nasiri-Boroujeni S, Lorigooini Z, Nazari M, Sadeghian R, Rafieian-Kopaei M, et al. Anchusa italica Retz. Hydro-Alcoholic Extract through Attenuation of Oxidative Stress Exerts an Anticonvulsant Effect on the Pentylenetetrazole-Induced Seizure in Mice. Int J Epilepsy 2021;07(02):052-8. doi:10.1055/s-0041-1742275
25. Peker E, Elpek GÖ. The Effect of Ellagic Acid on Intra-abdominal Adhesions Caused by Gallstones. Surg Laparosc Endosc Percutan Tech 2021;32(2):166-71. doi:10.1097/sle.0000000000001019
26. Khalili-Tanha G, Khalili-Tanha N, Nazari SE, Chaeichi-Tehrani N, Khazaei M, Aliakbarian M, et al. The Therapeutic Potential of Targeting the Angiotensin Pathway as a Novel Therapeutic Approach to Ameliorating Post-surgical Adhesions. Curr Pharm Des 2022;28(3):180-6. doi:10.2174/1381612827666210625153011
27. Majnoon S, Asgharzadeh F, Sabbaghzadeh R, Nazari SE, Yarmohammadi Z, Saeedi N, et al. Targeting Angiotensin-converting Enzyme Inhibitor via Enalapril Reduces Postsurgical Adhesion Band Formation. Lett Drug Des Discov 2024;21(17):3886-93. doi:10.2174/0115701808293346240726110944
28. Wang R, Guo T, Li J. Mechanisms of Peritoneal Mesothelial Cells in Peritoneal Adhesion. Biomolecules 2022;12(10):1498. doi:10.3390/biom12101498
29. Li P, Zhou H, Tu T, Lu H. Dynamic exacerbation in inflammation and oxidative stress during the formation of peritendinous adhesion resulted from acute tendon injury. J Orthop Surg Res 2021;16(1):293. doi:10.1186/s13018-021-02445-y
30. Hu Q, Xia X, Kang X, Song P, Liu Z, Wang M, et al. A review of physiological and cellular mechanisms underlying fibrotic postoperative adhesion. Int J Biol Sci 2021;17(1):298-306. doi:10.7150/ijbs.54403
31. Ghadiri M, Baradaran Rahimi V, Moradi E, Hasanpour M, Clark CCT, Iranshahi M, et al. Standardised pomegranate peel extract lavage prevents postoperative peritoneal adhesion by regulating TGF-β and VEGF levels. Inflammopharmacology 2021;29(3):855-68. doi:10.1007/s10787-021-00819-6
32. Özler M, Ersöz N, Özerhan İH, Topal T, Öter Ş, Korkmaz A. The effect of alpha-lipoic acid in the prevention of peritoneal adhesions. Turk J Gastroenterol 2011;22(2):190-4. doi:10.4318/tjg.2011.0190
33. Shahidi S, Komaki A, Raoufi S, Salehi I, Zarei M, Mahdian M. The Anti-nociceptive Effect of Ellagic Acid in Streptozotocin-induced Hyperglycemic Rats by Oxidative Stress Involvement. Basic Clin Neurosci 2021;12(6):861-72. doi:10.32598/bcn.2021.2413.1
34. Mirzaie Z, Bastani A, Haji-Aghamohammadi AA, Rashidi Nooshabadi M, Ahadinezhad B, Khadem Haghighian H. Effects of Ellagic Acid on Oxidative Stress Index, Inflammatory Markers and Quality of Life in Patients With Irritable Bowel Syndrome: Randomized Double-blind Clinical Trial. Clin Nutr Res 2022;11(2):98-109. doi:10.7762/cnr.2022.11.2.98
35. Asaad GF, Hassan A, Mostafa RE. Anti-oxidant impact of Lisinopril and Enalapril against acute kidney injury induced by doxorubicin in male Wistar rats: involvement of kidney injury molecule-1. Heliyon 2021;7(1):e05985. doi:10.1016/j.heliyon.2021.e05985
36. Andrade-Sierra J, Morales-Guillén ML, García-Sánchez A, Díaz-de la Cruz EN, Cerrillos-Gutiérrez JI, Rojas-Campos E, et al. The Effect of Enalapril, Losartan, or Not Antihypertensive on the Oxidative Status in Renal Transplant Recipients. Oxid Med Cell Longev 2022;2022:5622626. doi:10.1155/2022/5622626
37. Ghosh SS, Krieg R, Massey HD, Sica DA, Fakhry I, Ghosh S, et al. Curcumin and enalapril ameliorate renal failure by antagonizing inflammation in 5/6 nephrectomized rats: role of phospholipase and cyclooxygenase. Am J Physiol Renal Physiol 2012;302(4): F439-54. doi:10.1152/ajprenal.00356.2010
38. Walter T, Szabo S, Kazmaier S, Suselbeck T, Borggrefe M, Hoffmeister HM. Effect of ACE inhibition on the fibrinolytic system in patients requiring coronary artery bypass grafting. Thorac Cardiovasc Surg 2009;57(6):368-71. doi:10.1055/s-0029-1185596