ORIGINAL ARTICLE

THE EFFECT OF HAZELNUT OIL ON INTRA-ABDOMINAL ADHESION: AN EXPERIMENTAL STUDY IN A RAT MODEL

Fındık Yağının Batın İçi Yapışıklıklara Etkisi: Rat Modelinde Deneysel Çalışma

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ABSTRACT

Objective: Intra-abdominal adhesions are a common complication of abdominopelvic surgery, contributing to chronic pain, infertility, and intestinal obstruction. Oxidative stress and inflammation play central roles in their pathogenesis, underscoring the need for effective preventive agents with antioxidant and anti-inflammatory properties. This study aimed to evaluate the potential anti-adhesive effects of topically applied hazelnut oil compared to Seprafilm in a standardised rat model of peritoneal injury.

Material and Methods: Twenty-eight Sprague-Dawley rats were randomly assigned to four groups: Sham (hazelnut oil only), Adhesion (injury without treatment), Adhesion + Hazelnut Oil, and Adhesion + Seprafilm. Adhesions were induced via standardised cecal abrasion. Hazelnut oil (5 mL) or Seprafilm (30 × 20 mm) was applied intraperitoneally. After 14 days, macroscopic adhesions were scored using the Evans classification, and histopathological evaluation was conducted using the Zühlke score. Data were analyzed using the Kruskal-Wallis test.

Results: Significant differences were observed in macroscopic (Evans Score) and histopathological (Zühlke Score) adhesion scores among groups ($p < 0.001$). The Sham group exhibited significantly lower scores than the Adhesion group ($p < 0.001$). The Hazelnut Oil and Seprafilm groups showed lower median scores compared to the Adhesion group, but these differences were not statistically significant ($p > 0.05$). The Hazelnut oil showed a trend toward reduced histopathological fibrosis, similar to Seprafilm, suggesting a potential protective effect.

Conclusion: These findings suggest that hazelnut oil may have a role in reducing intra-abdominal adhesions, though the effect was not statistically significant in this small sample. Its natural composition and potential biochemical benefits warrant further investigation as a cost-effective anti-adhesive agent.

Keywords: *Intraabdominal Adhesions; Hazelnut Oil; Seprafilm; Antioxidants; Peritoneal Injury; Rat Model*

ÖZET

Amaç: İntraabdominal adezyonlar, abdominopelvik cerrahilerin sık görülen komplikasyonlarından biridir ve kronik ağrı, infertilite ve intestinal obstrüksiyon gibi ciddi klinik sonuçlara yol açabilir. Oksidatif stres ve inflamasyon bu sürecin patogenezinde merkezi bir rol oynamaktadır. Bu nedenle, antioksidan ve anti-inflamatuar özelliklere sahip etkili önleyici ajanlara ihtiyaç duyulmaktadır. Bu çalışmada, peritoneal yaralanma modeli oluşturulan sıçanlarda, topikal olarak uygulanan fındık yağının anti-adezif potansiyeli Seprafilm ile karşılaştırmalı olarak değerlendirilmiştir.

Gereç ve Yöntemler: Yirmi sekiz Sprague-Dawley cinsi sıçan rastgele dört gruba ayrılmıştır: Sham (yalnızca fındık yağı uygulanan), Adezyon (yaralanma ancak tedavi uygulanmayan), Adezyon + Fındık Yağı ve Adezyon + Seprafilm grupları. Adezyonlar, standartize edilmiş çekal abrazyon yöntemi ile indüklenmiştir. Fındık yağı (5 mL) ya da Seprafilm (30 × 20 mm) intraperitoneal olarak uygulanmıştır. On dört gün sonra makroskopik adezyonlar Evans sınıflandırması ile değerlendirilmiş, histopatolojik inceleme ise Zühlke skoru kullanılarak yapılmıştır. Veriler Kruskal-Wallis testi ile analiz edilmiştir.

Bulgular: Makroskopik (Evans skoru) ve histopatolojik (Zühlke skoru) adezyon derecelerinde gruplar arasında anlamlı fark saptanmıştır ($p < 0,001$). Sham grubunun skorları, Adezyon grubuna kıyasla anlamlı olarak daha düşük bulunmuştur ($p < 0,001$). Fındık Yağı ve Seprafilm gruplarının medyan skorları Adezyon grubuna göre daha düşük olmasına rağmen, bu farklar istatistiksel olarak anlamlı bulunmamıştır ($p > 0,05$). Fındık yağı, Seprafilm ile benzer şekilde histopatolojik fibrozisi azaltma eğilimi göstermiştir.

Sonuç: Bu bulgular, fındık yağının intraabdominal adezyonların azaltılmasında potansiyel bir role sahip olabileceğini göstermektedir. Her ne kadar bu çalışma istatistiksel anlamlılık ortaya koymasa da, fındık yağının doğal içeriği ve biyokimyasal faydaları göz önüne alındığında, maliyet etkin bir anti-adezif ajan olarak daha kapsamlı araştırmalara konu edilmesi gerektiği düşünülmektedir.

Anahtar Kelimeler: *İntraabdominal Adezyonlar; Fındık Yağı; Seprafilm; Antioksidanlar; Peritoneal Yaralanma; Rat Modeli*

INTRODUCTION

Intra-abdominal adhesions remain one of the most pervasive yet underappreciated complications of abdominal and pelvic surgeries. Affecting up to 90% of patients undergoing open abdominal procedures, they contribute substantially to postoperative morbidity and ascending morbidity (1). These fibrous bands, formed as aberrant healing responses between adjacent peritoneal surfaces, are implicated in a broad spectrum of clinical consequences, including small bowel obstruction, which comprises nearly 75% of all such cases, infertility in women, chronic pelvic pain, and significant technical challenges during reoperations (2). Furthermore, the cumulative economic burden from adhesion-related complications is staggering, with billions spent annually on hospital readmissions, fertility treatments, and surgical revisions (3). Despite considerable surgical and pharmaceutical advances, there is still no universally accepted method to prevent their formation effectively.

The pathophysiology of adhesion formation is complex and multifactorial, involving surgical trauma, local inflammation, oxidative stress, and impaired fibrinolysis (4). Initial peritoneal injury disrupts mesothelial integrity, triggering exudation of fibrin-rich plasma and recruitment of inflammatory cells. Under normal conditions, fibrin deposits are degraded by peritoneal fibrinolytic activity; however, in the setting of oxidative and inflammatory stress, this balance is disrupted, leading to the development of fibrous encapsulation and adhesion (5). Notably, the role of reactive oxygen species (ROS) is critical, as they not only damage peritoneal cells but also inhibit tissue plasminogen activator (tPA), exacerbating adhesion progression (6,7). Targeting oxidative pathways and inflammatory mediators has therefore emerged as a promising strategy in adhesion prevention (8). In recent years, attention has shifted to natural compounds with antioxidant and anti-inflammatory properties, including plant-derived oils, due to their potential therapeutic benefits (9). Hazelnut oil, extracted from Corylus avellana, is rich in oleic and linoleic acids, tocopherols, and phenolic compounds—biomolecules known to mitigate oxidative stress and modulate inflammatory responses (10-12). Although previous studies have investigated the health benefits of hazelnut oil, its possible application in the prevention of intra-abdominal adhesions remains unexplored.

This study aimed to evaluate the macroscopic and histopathological effects of intraperitoneally applied hazelnut oil in a standardised rat model of peritoneal injury, thereby contributing novel insights to the search for effective and biocompatible anti-adhesive agents.

MATERIALS AND METHODS

This study was approved by the Ordu University Animal Ethics Committee (Approval No: OU-HADYEK-2020/13) and adhered to national guidelines for laboratory animal care. Twenty-eight healthy male Sprague-Dawley rats (8–12 weeks old, 250–300 g) were housed under standard conditions (21 ± 2°C, 12-hour light/dark cycle, 40–60% humidity) with ad libitum access to water and standard chow. Rats were randomly assigned to four groups (n=7 per group).

Group 1 (Sham): 5 mL of hazelnut oil was administered intraperitoneally without laparotomy.

Group 2 (Adhesion): Laparotomy with standardised cecal abrasion to induce adhesions.

Group 3 (Adhesion + Hazelnut Oil): Laparotomy, cecal abrasion, and 5 mL intraperitoneal hazelnut oil.

Group 4 (Adhesion + Seprafilm): Laparotomy, cecal abrasion, and placement of a 30 × 20 mm Seprafilm (Genzyme, USA). Seprafilm was placed to cover the abraded cecal surface, ensuring contact with peritoneal fluid to secure adhesion. Its position was verified before abdominal closure.

Rats were anesthetised with intraperitoneal ketamine (50 mg/kg, Ketalar, Pfizer, Turkey) and xylazine (7 mg/kg, Rompun, Bayer, Turkey). The abdominal skin was shaved and disinfected with povidone-iodine. A 3 cm midline incision was made, and the cecum was exteriorised and abraded with sterile dry gauze to induce serosal petechiae. Treatments were applied as per group assignments, and the abdominal wall was closed with 2/0 PDS sutures (fascia) and 3/0 silk sutures (skin). Postoperative analgesia was provided with 0.02 mg/kg subcutaneous fentanyl. Oral feeding resumed post-recovery.

Refined hazelnut oil (Çotanak, Türkiye) was sterilised via filtration through a 0.45 µm filter. The pH was adjusted to 6.8, matching peritoneal dialysis fluid (to match physiological peritoneal pH).

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On postoperative day 14, rats were euthanised under anaesthesia, and a U-shaped laparotomy was performed. Adhesions were scored by a blinded surgeon using the Evans classification (Table 1).

Tissue samples (~2 g) from adhesion sites (cecum and abdominal wall) were fixed in 10% formalin, embedded in paraffin, and sectioned at 5 µm. Sections were stained with hematoxylin and eosin (H&E) and evaluated by a blinded pathologist using the Zühlke scoring system (Table 2).

All data were analysed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Due to the small sample size and ordinal nature of the data, non-parametric statistical methods were used. Comparisons among groups were performed using the Kruskal–Wallis test, and if statistically significant, pairwise comparisons were carried out using the Mann–Whitney U test with Bonferroni correction. A p-value less than 0.05 was considered statistically significant.

RESULTS

One rat each from Groups 1, 2, and 3, and two from Group 4, died postoperatively and were excluded, resulting in n = 6 (Groups 1–3) and n = 5 (Group 4).

Significant differences were observed in Evans Scores among groups (Kruskal-Wallis, H = 16.624, df = 3, p < 0.001; Table 3). Post-hoc Dunn's tests showed Group 1 (Sham, median = 0, IQR = 0–0) had significantly lower scores than Group 2 (Adhesion, median = 2.5, IQR = 2–3) (p < 0.001). Group 3 (Adhesion + Hazelnut Oil, median = 1.5, IQR = 1–2) and Group 4 (Adhesion + Seprafilm, median = 2, IQR = 1–2) had lower median scores than Group 2, but differences were not significant (p = 0.500 and p = 0.393, respectively). No significant difference was found between Groups 3 and 4 (p = 1.000). Mean ranks were 3.5 (Group 1), 18.5 (Group 2), 10.0 (Group 3), and 12.0 (Group 4).

Similar patterns were observed for Zühlke Scores (Kruskal-Wallis, H = 16.944, df = 3, p < 0.001; Table 4). Group 1 had significantly lower fibrosis scores than

Table 1. Evans' Classification of Adhesion Severity and Extent

Stage	Area Score	Resistance Score
0	No adhesions	No adhesions
1	Adhesion area under 25%	Adhesions separating spontaneously
2	Adhesion area between 25-50%	Adhesions are separated with traction
3	Adhesion area over 50%	Adhesions requiring dissection for separation

Table 2. Zühlke Scoring System

Grade	
0	No adhesions, no inter-tissue reaction developed
1	Loose connective tissue, sparse cells, old and new fibrin, thin reticulin fibres
2	Connective tissue with few cells and capillaries
3	Thicker connective tissue, dense cells, more prominent and thicker-walled vessels, sparse elastic and smooth muscle fibres, sparse collagen fibres
4	Thick or nodular granulation tissue, dense collagen fibres and smooth muscle fibres

Table 3. Macroscopic Evaluation of Intra-Abdominal Adhesions Using Evans Score

Evans' Score	Group 1 (n=6)	Group 2 (n=6)	Group 3 (n=6)	Group 4 (n=5)	P-value
0	5	-	-	-	<0.001
1	1	-	3	2	
2	-	3	3	3	
3	-	3	-	-	
Total Score	1	15	9	8	

Group 1 = Sham; Group 2 = Adhesion (laparotomy + saline); Group 3 = Adhesion + Hazelnut Oil; Group 4 = Adhesion + Seprafilm. Evans Score: 0 = no adhesions, 3 = dense adhesions requiring dissection.P-value derived from the Kruskal-Wallis test.

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Table 4. Histopathological Evaluation of Intra-Abdominal Adhesions Using Zühlke Score

Zühlke' Score	Group 1 (n=6)	Group 2 (n=6)	Group 3 (n=6)	Group 4 (n=5)	P-value
0	4	-	-	-	<0.001
1	2	-	1	1	
2	-	2	5	3	
3	-	3	-	-	
4	-	1	-	-	
Total Score	2	17	11	7	

Group 1 = Sham; Group 2 = Adhesion; Group 3 = Adhesion + Hazelnut Oil; Group 4 = Adhesion + Seprafilm. Zühlke Score: 0 = normal, 3 = dense fibrosis.P-value derived from the Kruskal-Wallis test.

Group 2 ($p < 0.001$). Groups 3 and 4 had lower median scores than Group 2; yet, the differences were not statistically significant ($p = 0.669$ and $p = 0.296$, respectively). No difference was found between Groups 3 and 4 ($p = 1.000$). Mean ranks were 4.0 (Group 1), 18.0 (Group 2), 10.5 (Group 3), and 11.5 (Group 4).

These findings suggest that both hazelnut oil and Seprafilm may exert a protective effect against peritoneal fibrosis, although not to the extent of the sham-operated condition. Representative histological images from Group 3 are presented in Figure 1, illustrating minimal fibrotic tissue and preserved serosal architecture. Similarly, Group 4 histopathology is shown in Figure 2, demonstrating a moderate reduction in inflammatory cell infiltration and collagen deposition compared to Group 2.

DISCUSSION

This study investigated the effect of topically applied hazelnut oil on intra-abdominal adhesion formation in a rat model of peritoneal injury. Our results demonstrated significant differences in both macroscopic and histopathological adhesion scores among groups ($p < 0.001$), with the Sham group exhibiting significantly lower scores compared to the Adhesion group ($p < 0.001$). The treatment groups, receiving either hazelnut oil or Seprafilm, showed lower median adhesion scores compared to the Adhesion group, though these differences were not statistically significant (Evans Score: $p = 0.500$ and $p = 0.393$; Zühlke Score: $p = 0.669$ and $p = 0.296$, respectively). This trend suggests a potential protective effect of hazelnut oil, particularly at the histological level, supporting its candidacy as a natural anti-adhesive agent, though further validation is needed.

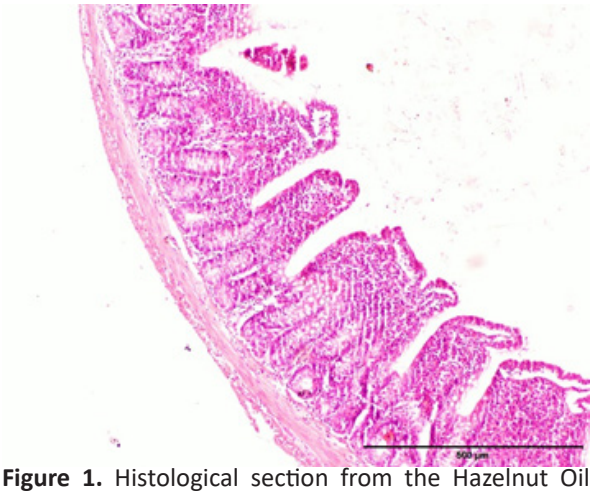

Figure 1. Histological section from the Hazelnut Oil group, showing minimal fibrous adhesion and preserved serosal architecture with limited inflammatory infiltration (H&E, ×100).

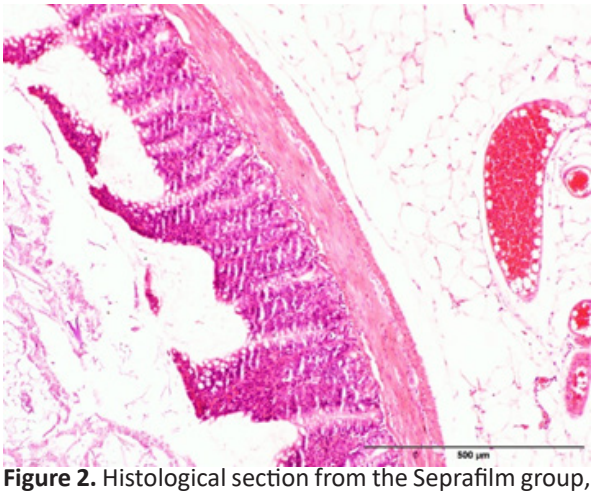

Figure 2. Histological section from the Seprafilm group, showing moderate serosal fibrosis with reduced inflammatory cell infiltration compared to the Adhesion group (H&E, ×100).

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Hazelnut oil's therapeutic potential is supported by its biochemical composition, notably its richness in monounsaturated fatty acids (especially oleic acid), tocopherols, and phenolic compounds. These constituents contribute to potent antioxidant and anti-inflammatory effects, which are critically important in adhesion pathogenesis. It is well established that oxidative stress and impaired fibrinolysis are key drivers in adhesion formation following peritoneal trauma (6,7). Hazelnut oil may mitigate reactive oxygen species (ROS)-induced mesothelial injury, preserve the fibrinolytic balance, and reduce fibroblast activation, as previously described (10, 12).

Our results notably showed that while macroscopic scores did not differ significantly, histopathological evaluation revealed a consistent shift toward lower Zühlke grades in the hazelnut oil group. This implies a less organised and less fibrotic adhesion structure, indicating that hazelnut oil may exert a more substantial impact at the microscopic level, potentially preventing the maturation of early adhesions. This distinction between gross and histological outcomes highlights the importance of comprehensive evaluation in adhesion studies and suggests that hazelnut oil may interfere with fibrosis at a subclinical level.

Comparative analysis with Seprafilm, a clinically approved mechanical barrier, further contextualises the findings. While Seprafilm aims to prevent adhesion by physical separation, hazelnut oil appears to act via biological mechanisms. Interestingly, our histological data indicated a trend toward better anti-fibrotic performance of hazelnut oil compared to Seprafilm, although this difference did not reach statistical significance. Our statement that the Hazelnut Oil group exhibited lower Zühlke scores compared to the Seprafilm group requires clarification, as the total histopathological score for Hazelnut Oil was higher than for Seprafilm. This numerical difference likely reflects the smaller sample size in the Seprafilm group (n=5) compared to the Hazelnut Oil group (n=6), which may have influenced the overall score. However, histological evaluation showed minimal fibrous adhesion and preserved serosal architecture in the Hazelnut Oil group, contrasted with moderate serosal fibrosis in the Seprafilm group. These findings suggest that hazelnut oil may reduce fibrotic maturation, supporting its potential as an anti-adhesive agent despite the lack of statistical significance.

This raises the possibility that biologically active oils could offer molecular-level benefits, and could even be considered as adjuncts to existing mechanical strategies (13). Similar multi-modal mechanisms have been observed with other natural agents, such as resveratrol and ligustrazine, both of which suppress oxidative and inflammatory cascades involved in adhesion formation (14, 15).

The present findings align with data from Kiyakli et al., where a similar downward trend was observed, although it was not statistically significant (16). Such alignment highlights the challenge of underpowered preclinical studies, where biological effects may be obscured by sample size limitations rather than a lack of efficacy. It also supports the growing paradigm that early-stage experimental models should focus not solely on p-values but also on histological and mechanistic trends as signals of therapeutic promise.

This study has limitations. First, the small sample size limited statistical power and may have prevented the detection of significant differences. Second, the study did not include biochemical assays to evaluate changes in oxidative stress markers, cytokine levels, or fibrinolytic mediators—data that could validate the proposed mechanisms of action. Third, while the 14-day follow-up allowed for the assessment of mature adhesions, it did not explore long-term recurrence or chronic remodelling. Finally, although the rat model is widely accepted in adhesion research, interspecies differences may limit direct clinical translation (17,18).

CONCLUSION

This study provides preliminary evidence that hazelnut oil may reduce intra-abdominal adhesions, though the effect was not statistically significant in this small sample. Its natural composition and potential biochemical benefits warrant further investigation as a cost-effective adjunctive therapy. Larger studies with molecular analyses and extended follow-up are needed to validate these findings and optimize clinical application.

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