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Efficacy of water–based propolis in preventing intra–abdominal adhesions in an experimental rat model

El uso eficaz del propóleo hidrosoluble en la prevención de adherencias intraabdominales en un modelo experimental de ratas

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ABSTRACT

Intra–abdominal adhesions are one of the most common postoperative complications following surgical procedures. Globally, it is among the leading causes of hospital readmissions, chronic pain, and serious conditions such as infertility in both human and veterinary medicine. The risk of development is particularly high after pelvic and abdominal surgeries. Despite this common condition, there is still no effective and reliable treatment method to prevent adhesions. This study aims to evaluate the potential effect of propolis (both oral and intra–abdominal) with its anti–inflammatory and antioxidant properties in the prevention of intra–abdominal adhesions. The rats used in the study were divided into five: Healthy Control Group , Control Group , Sham Group , Oral Propolis Group , and Intra–abdominal Propolis Group . After the intra–abdominal adhesion model was established in rats, excluding the Healthy Control Group and Sham Group, rats in the Oral Propolis Group were administered 75 mg·kg^{-1} of propolis orally once daily for 20 days, while rats in the Intra–abdominal Propolis Group received a single dose of 75 mg·kg^{-1} of propolis intra–abdominally. Results showed that the Oral Propolis Group and Intra–abdominal Propolis Group were statistically significantly lower than the Control Group in terms of macroscopic adhesion scores. Although there was no statistically significant difference when the Oral Propolis Group and Intra–abdominal Propolis Group were compared with the Control Group in terms of fibrosis, it was observed that the Intra–abdominal Propolis Group was statistically significantly lower than the Control Group in terms of inflammation severity. Biochemical analyses, it was revealed that the oxidative stress parameters of rats in both oral and intra–abdominal propolis application were statistically different from the Control Group and that these two were close to the Healthy Control Group in terms of oxidative stress. As a result, it was concluded that both intra–abdominal and oral propolis applications prevent the formation of intra–abdominal adhesions and can be used for prophylactic purposes after abdominal and pelvic operations.

Key words: Propolis; intra–abdominal adhesion; fibrin; rat

RESUMEN

Las adherencias intraabdominales son una de las complicaciones postoperatorias más comunes después de procedimientos quirúrgicos. A nivel mundial, se encuentran entre las principales causas de reingresos hospitalarios, dolor crónico y afecciones graves como la infertilidad, tanto en la medicina humana como en la veterinaria. El riesgo de desarrollo es particularmente alto después de cirugías pélvicas y abdominales. A pesar de ser una condición común, aún no existe un método de tratamiento eficaz y confiable para prevenir las adherencias. Este estudio tiene como objetivo evaluar el efecto potencial del propóleo (administrado por vía oral e intraabdominal), gracias a sus propiedades antiinflamatorias y antioxidantes, en la prevención de adherencias intraabdominales. Las ratas utilizadas en el estudio se dividieron en cinco grupos: Grupo Control Saludable, Grupo Control, Grupo Simulado, Grupo de Propóleo Oral y Grupo de Propóleo Intraabdominal. Después de establecer el modelo de adhesión intraabdominal en las ratas, excluyendo los Grupo Control Saludable y Grupo Simulado, a las ratas del Grupo de Propóleo Oral se les administró 75 mg·kg^{-1} de propóleo por vía oral una vez al día durante 20 días, mientras que a las ratas del Grupo de Propóleo Intraabdominal se les administró una dosis única de 75 mg·kg^{-1} de propóleo por vía intraabdominal. Los resultados mostraron que los Grupo de Propóleo Oral y Grupo de Propóleo Intraabdominal presentaron puntuaciones de adherencias macroscópicas estadísticamente menores que el Grupo Control. Aunque no hubo diferencias estadísticamente significativas en cuanto a fibrosis al comparar los Grupo de Propóleo Oral e Grupo de Propóleo Intraabdominal con el Grupo Control, se observó que el grupo IPG presentó una severidad de inflamación significativamente menor que el Grupo Control. En los análisis bioquímicos, se reveló que los parámetros de estrés oxidativo de las ratas de los grupos con aplicación de propóleo, tanto oral como intraabdominal, fueron estadísticamente diferentes respecto al Grupo Control y que estos dos grupos se acercaron al Grupo Control Saludable en términos de estrés oxidativo. Como conclusión, se determinó que tanto la aplicación intraabdominal como la oral de propóleo previenen la formación de adherencias intraabdominales y pueden utilizarse con fines profilácticos tras operaciones abdominales y pélvicas.

Palabras clave: Propóleo; adherencia intraabdominal; fibrina; rata

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INTRODUCTION

The peritoneum is a serous membrane that lines the inner surface of the abdominal cavity and allows the abdominal organs to move smoothly without rubbing against each other or the abdominal wall. It prevents the formation of adhesions of different abdominal organs by preventing blood clotting in the abdominal cavity through the effect of plasminogen activators secreted by the mesothelial cells present in its structure. Tissue ischemia, serosal injuries and infections may reduce the effect of plasminogen activators and cause fibrin production in the abdominal cavity. This condition, which makes the movement of organs within the abdominal cavity difficult, is called intra–abdominal adhesion [1, 2, 3, 4, 5, 6].

Although intra–abdominal adhesions occur in the majority of patients after abdominal and pelvic operations, clinical symptoms are encountered in a small portion of these patients. Infertility, intra–abdominal abscesses, small bowel obstructions and chronic pain are the most important health problems encountered following intra–abdominal adhesions [1, 2, 3, 4, 5, 6, 7]. Many herbal extracts [8], enzyme inhibitors [9], chemical substances [4,10] and biomaterials [11], have been used to prevent intra–abdominal adhesions since long.

Propolis is produced by honeybees (*Apis mellifera*) collecting the buds, resins and sap of plants and processing them with their own enzymes. Propolis contains many compounds, especially pharmacologically valuable flavonoids and phenolic compounds. It is also known that propolis has antibacterial, antiviral, antifungal, anti–inflammatory, immunomodulatory and antioxidant properties due to the active ingredients present in it [12, 13, 14, 15].

Compounds such as caffeic acid, quercetin, naringenin, and caffeic acid phenyl ester (CAPE) found in propolis contribute to its anti–inflammatory effect by suppressing the synthesis of prostaglandins and leukotrienes (inflammatory molecules) produced by macrophages. The compounds present in propolis also have an inhibitory effect on enzymes such as myeloperoxidase, NADPH–oxidase, ornithine decarboxylase, and tyrosine protein kinase [14, 16]. Propolis prevents oxidative stress through its polyphenol compounds that eliminate excess free radicals from the body [17].

The CAPE compound, identified as one of the main active ingredients of propolis, exhibits antioxidant and anti–inflammatory effects. It reduces the increased malondialdehyde (MDA) level in the final stage of lipid peroxidation by suppressing free radical production [18].The most important mechanisms for the anti–inflammatory effects of CAPE compound are its significant suppression of cyclooxygenase-2 (COX-2) expression and its strong inhibition of Nuclear Factor kB (NF–kB) activation [19].

In this study, the effectiveness of propolis, which contains many anti–inflammatory agents, especially CAPE, in preventing intra–abdominal adhesions was investigated. In the study, two separate treatment groups were created and water–based propolis was administered orally to one group and intra–abdominally to the other group, and the effectiveness of different application methods in preventing intra–abdominal adhesion was evaluated.

MATERIALS AND METHODS

Experimental rats

In this study, 39 Sprague Dawley rats (*Rattus norvegicus*) were used. The experiments were conducted between November and December 2024. In the study, 8-week–old female Sprague Dawley rats weighing an average of 250-300 g were used. Rats were included in the study during the diestrus phase of the estrous cycle.

The rats were housed under standard laboratory conditions with a temperature of 22 ± 2°C, humidity of 50-60%, and a 12-hour light/dark cycle. The animals were kept in cages with 3-4 rats each and were given free access to standard pelleted feed and water. After the acclimatization period of 10 days (d), experimental rats were randomly assigned to one of the five experimental groups. In the study, the groups were defined as Healthy Control Group (HCG), Control Group (CG), Oral Propolis Group (OPG), Intra–abdominal Propolis Group (IPG), and Sham Group (SG). The HCG group consisted of 7 rats and the other four groups consisted of 8 rats each.

Creation of intraabdominal adhesion model

In the rats of the CG, OPG, and IPG groups, an adhesion model was created, whereas in the SG group, laparotomy was performed without creating an adhesion model. To induce anesthesia in the rats in the groups to be operated (CG, OPG, IPG, and SG), 8 $mg \cdot kg^{-1}$ xylazine hydrochloride was administered intramuscularly. Then, 10 min later, 80 $mg \cdot kg^{-1}$ ketamine hydrochloride was administered intramuscularly. No surgical procedure or treatment was applied to the rats in the HCG group. After being fixed in the supine position on the operating table, the rats in the groups where the adhesion model was to be created (CG, OPG, and IPG) as well as those in the SG group had their abdominal midline shaved and cleaned prior to surgery. After the application of 10% povidone–iodine solution, the area was prepared for the operation by limiting it with sterile drapes. An approximately 2 cm long skin incision was made along the median line of the rats using a #15 blade with a slight curve.

Laparotomy was performed by making an incision on the linea alba, and the cecum was exteriorized through the incision site using a mini retractor (Army–Navy Retractor). Using a separate sterile toothbrush for each animal, abrasion was performed on the cecum until serosal hemorrhage occurred over an approximately 1 cm^2 area. Then, the same scraping operations were performed on the visceral surface of the abdominal wall in a place close and opposite to the area where the scraping was performed on the cecum, creating a standard adhesion model. In the three groups where the intra–abdominal adhesion model was created (CG, OPG, and IPG) as well as in the SG group, surgical incisions were closed with simple interrupted sutures using USP 4/0 Vicryl thread, in accordance with standard surgical procedures (FIG.1) [7]. A single dose of Meloxicam at 2 $mg \cdot kg^{-1}$ was administered subcutaneously to the rats during the postoperative period.

Intraabdominal and oral propolis applications

After the operation, 75 $mg \cdot kg^{-1}$ of water–based propolis, diluted to 0.5 mL with saline solution (Concentration of the propolis stock solution: 25 $mg \cdot ml^{-1}$, Geographical source: Erdemli region of Mersin, Turkey; Botanical origin: *Populus* and *Pinaceae* spp.),

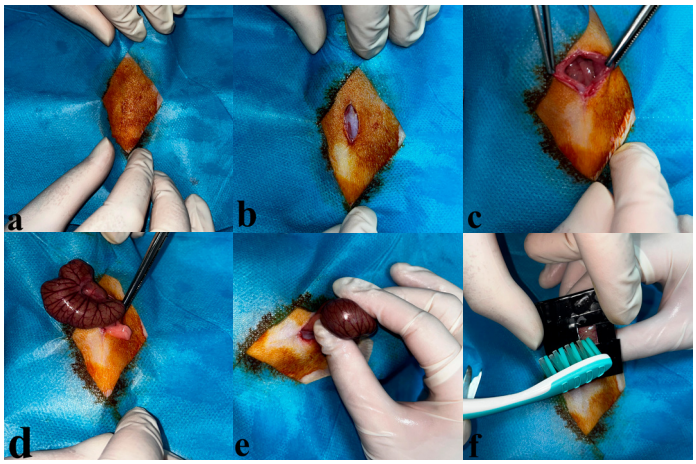

FIGURE 1. The steps for establishing the experimental intra–abdominal adhesion model are as follows: preparation of the operative field (a), skin incision (b), incision of the linea alba (c), exteriorization of the cecum through the incision line (d, e), and abrasion of a 1 cm² area on the cecum (f)

was administered intra–abdominally to the rats in the IPG group before closing the abdominal cavity. In the OPG group, rats were administered 75 mg·kg^{-1} of water–based propolis, diluted to 0.5 mL with saline solution, once daily by gavage for 20 d. The 75 mg·kg^{-1} dose used in the study was selected as an average dose based on data obtained from previous studies in the literature [20, 21]. No application was made to the rats in the CG and SG groups after the operation. No application was made to the rats in the HCG group at any stage of the study.

Determination of macroscopic adhesion score

For macroscopic evaluation of intraabdominal adhesions, the macroscopic adhesion grading criteria of Nair *et al*. [22] were used. According to these criteria, the intra–abdominal adhesions were macroscopically scored from 0 to 4, as described in TABLE I and FIG. 2.

Histopathological examination

Samples taken from the inflamed area tissue on the cecum and abdominal cavity were fixed in 10% neutral formalin solution for at least 24 h. The fixed tissues were embedded in paraffin blocks after undergoing standard tissue tracking procedures.

TABLE I
Macroscopic Adhesion Grading Criteria

Score	Criteria (Clinical findings)
0	No adhesion
1	A single band of adhesion between organs or between an organ and the peritoneum
2	Two adhesion bands between organs or between an organ and the peritoneum
3	More than two adhesive bands between organs or between the organ and the abdominal wall or adhesion of intestinal serosa without adhesion to the abdominal wall
4	The abdominal organs are directly attached to the abdominal wall

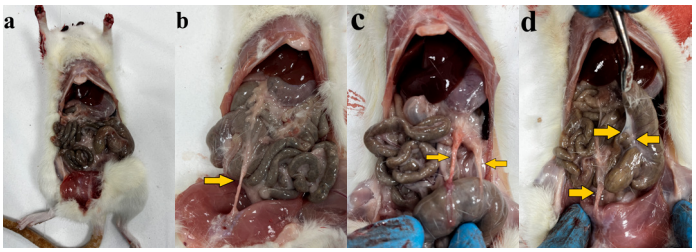

FIGURE 2. Macroscopic Evaluation Score. Score 0: (No adhesion, a), Score 1: (A single band of adhesion between organs or between an organ and the peritoneum, b), Score 2: (More than two adhesive bands between organs or between the organ and the abdominal wall or adhesion of intestinal serosa without adhesion to the abdominal Wall, c), Score 3: (More than two adhesive bands between organs or between the organ and the abdominal wall or adhesion of intestinal serosa without adhesion to the abdominal Wall, d).

After 5 μm–thick sections were obtained from the paraffin blocks using a microtome (HM325, Thermo Scientific, Waltham, MA, USA), the sections were placed onto slides. The sections were examined under a light microscope (Leica Microsystems, Wetzlar, DM 750, Germany) after applying Hematoxylin–Eosin staining for histopathological examination. The sections were also stained according to the procedure of the Atom Scientific Masson Trichrome (Methyl Blue) Stain Kit (RRSK20-100, StatLab, USA) Staining kit, and the necessary areas were photographed. As a result of the examinations, the severity of inflammation and fibrosis were scored between 0–3 according to the scoring of Celepli *et al*. [23], as described in TABLE II.

TABLE II
Histopathological scoring of adhesions

Score	Inflammation Severity	Fibrosis Severity
0	None	None
1	Multinucleated giant cells, lymphocytes and plasma cells	Mild
2	Multinucleated giant cells, plasma cells, eosinophils and neutrophils	Moderate
3	Inflammatory cell infiltration and microabscess presence	Severe

Biochemical examination

At the end of the experiment, blood samples were collected into EDTA–containing tubes from the rats in both the control and experimental groups, after which they were euthanized by decapitation under anesthesia with xylazine hydrochloride (Rompun®, 23.32 mg·mL^{-1}; Bayer HealthCare, Leverkusen, Germany). Blood samples collected in EDTA tubes were centrifuged at 1630 G for 15 min using a refrigerated centrifuge (NF800R, Nüve, Türkiye) to obtain plasma. Plasma was used to measure MDA, a lipid peroxidation marker, while whole blood was employed for determining GSH and GSH–Px activities. Following plasma separation, blood samples were rinsed thrice with 0.9% NaCl saline. During the washing phase, blood samples were centrifuged (NF800R Santrifüj Cihazi, Nüve, Türkiye) at 18620 G for 10 min, and the upper portion was discarded. After the third wash, hemoglobin (Hb) levels, the activity of Catalase (CAT) and the Superoxide Dismutase (SOD) activities were determined in the erythrocyte packet remaining at the bottom.

Tissue MDA levels were assessed by spectrophotometry (Thermo Scientific Genesys 10S UV–VIS, USA) using a modified Placer *et al.* [24] method. The method involves the interaction between thiobarbituric acid (TBA) and MDA, which is a by product of lipid peroxidation. The Reduced Glutathione (GSH) levels were measured using amethod reported by Ellman *et al.* [25], which is based on the spectrophotometric determination of the yellow color formed when 5.5'–dithiobis–2–nitrobenzoik asit (DTNB) is added to sulfhydryl groups. CAT enzyme was determined by the spectrophotometric method of Aebi [26], based on the breakdown of H_2O_2, a compound absorbing light at 240 nm. The Beutler method [27] was employed to assess Glutathione Peroxidase (GSH–Px) activity by measuring the conversion of GSH to Glutathione disulfide (GSSG) catalyzed by GSH–Px in the presence of H_2O_2, with GSSG formation tracked through the GR reaction.SOD activity was determined using a modified method by Sun *et al.* [28], which involves the reduction of nitroblue tetrazolium (NBT) by the superoxide anion produced by the xanthine oxidase system, and the color of the reduction product was evaluated as SOD activity. Hemoglobin concentrations were assessed via the Drabkin method according to Frankel *et al.* [29]. Hemoglobin levels were measured to determine the specific activities of the enzymes whose activities were determined in the study.

Statistical analysis

SPSS (version 22.0) program was used for statistical evaluation. Since macroscopic and biochemical parameters did not show normal distribution, comparison of mean differences between groups was made using Kruskal–Wallis test, and comparison of differences between two groups was made using Mann–Whitney U test. Since histopathological data showed normal distribution, mean differences between groups were made using One Way ANOVA test and pairwise comparisons between groups were made using Tukey posthoc test. Data are presented as mean ± SEM value. $P<0.05$ value was accepted as significant [30].

RESULTS AND DISCUSSION

In studies on intra–abdominal adhesion, the creation of the adhesion model is a very important stage among the conditions affecting the results. The most commonly used intra–abdominal adhesion models include the classical sac model (cecum–sidewall model), serosal abrasion model, ischemia–reperfusion model and chemical irritant model [31, 32]. Nian *et al.* [32] reported that the classical sac model for rats is a stable and standardized model and has better usability. In this study, as in many previous investigations, the classical pouch model was employed to facilitate standardization across experiments.

Macroscopic and histopathological findings

In this study, mean macroscopic adhesion score was significantly lower in SG, OPG and HCG groups compared to CG group ($P<0.05$). There was statistically non–significant difference in macroscopic adhesion score between the HCG and OPG and SG groups. The adhesion severity of the rats in the IPG group was less and statistically significant compared to the rats in the CG group where adhesion was created but no treatment was applied. In short, it was seen that both oral and intra–abdominal water–based propolis applications reduced the adhesion severity statistically significantly (TABLE III).

In the evaluation made in terms of histopathological findings, it was found that fibrosis was more severe in rats applied oral and intra–abdominal propolis (OPG and IPG groups) compared to the CG group in which the adhesion model was created, but there was no statistical difference. However, fibrosis severity was significantly reduced in SG group compared to CG group ($P<0.05$). When evaluated in terms of inflammation severity, it was found that the inflammation severity was less in the rats in the IPG group compared to the rats in the CG group and was statistically significant. Again, although the inflammation severity was less in the rats in the OPG group compared to the rats in the CG group, there was no statistical difference between them (TABLE III), (FIG. 3)

TABLE III
Statistical analysis of macroscopic adhesion score, inflammation and fibrosis findings according to groups

	CG	SG	OPG	IPG	HCG	*P*
Macroscopic Score (0–4)	1.75 ± 0.36^{a}	0.5 ± 0.26^{bc}	0.25 ± 0.16^{b}	1.0 ± 0.26^{ac}	0.00 ± 0.00^{b}	<0.05
Inflammation Score (0–3)	1.38 ± 0.32^{a}	0.00 ± 0.00^{b}	1.25 ± 0.41^{a}	0.88 ± 0.13^{ab}	0.00 ± 0.00^{b}	<0.05
Fibrosis Score (0–3)	1.38 ± 0.18^{a}	0.25 ± 0.16^{b}	1.63 ± 0.26^{a}	1.75 ± 0.25^{a}	0.00 ± 0.00^{b}	<0.05

The increase in the scores is observed to reflect the progressive severity of adhesion, the intensification of the inflammatory response, and the marked increase in fibrotic tissue formation. In the study, the groups were defined as Control Group: (CG), Sham Group: (SG), Oral Propolis Group: (OPG), Intra–abdominal Propolis Group: (IPG) and Healthy Control Group: (HCG), significance: (*P*)

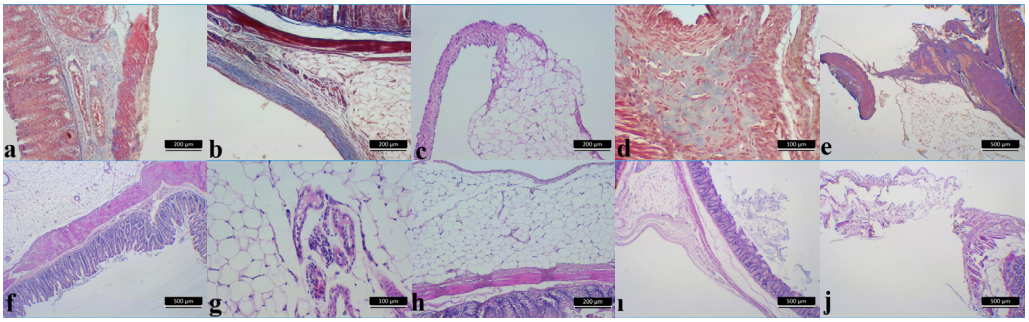

FIGURE 3. Histopathological images of the ceca of rats in the HCG group (a, f); increased connective tissue in the subserosa of rats in the CG group (b), cellular infiltration in the subserosa of rats in the CG group (g); adhesion in the subserosa of rats in the SG group (c), increased connective tissue in the subserosa of rats in the SG group (h); increased connective tissue in the subserosa of rats in the OPG group (d, i); adhesion formation in rats in the IPG group (e, j)

In the study conducted by Günay *et al*. [9], an intra–abdominal adhesion model was established in rats, and intra–abdominal aprotinin and methylene blue were administered. It was reported that the macroscopic adhesion scores in these groups were statistically significantly lower than those of the control group. While it was determined that 86.6% of the rats in the aprotonin–applied group did not have adhesion formation, they reported that this rate was 46.6% in the methylene blue–applied group.

Sağliyan *et al.* [6] applied bovine amniotic fluid and flunixin meglumine intraperitoneally to rats in which they created an intra–abdominal adhesion model and reported that macroscopic adhesion scores in these groups were statistically significantly lower than in the control group. In the same study, they reported that there was no statistical difference between the groups in terms of inflammation and fibrosis findings in the histopathological evaluation.

Gümüşgerdanli [33], reported that macroscopic adhesion scores in rats administered oral rapamycin at a daily dose of 1 mg·kg^{-1} for 3 days before creating the intra–abdominal adhesion model were statistically significantly lower than in the control group. Again, the same study reported that there was no significant difference between the groups in terms of histopathology. Kabalar *et al.* [10] reported in their study in which they applied intraperitoneal boric acid to rats in which they created an intra–abdominal adhesion model that both macroscopically and microscopically adhesion scores were significantly lower in the boric acid–applied group compared to the control group.

Diken Allahverdi *et al.* [34], reported that in their study in which they applied intraperitoneal alpha–lipoic acid to rats in which they created an intra–abdominal adhesion model, the macroscopic adhesion score decreased statistically significantly compared to the control group.

Birben [14], reported in his study investigating the effectiveness of intraperitoneal propolis application in preventing postoperative peritoneal adhesions that the macroscopic adhesion score in the propolis group was statistically significantly higher than in the other groups. They reported that this situation may depend on the application method of propolis, the amount applied, and the high concentration of its solvent. In this study, it was found that intra–abdominal and oral propolis application to rats in which intra–abdominal adhesion was created with the classical pouch model reduced the macroscopic adhesion score at a statistically significant level. Again, in the histopathological evaluation, although there was no significant difference between the groups in terms of fibrosis severity, it was observed that the group with intra–abdominal propolis application had statistically significantly lower inflammation findings.

Furthermore, although the macroscopic adhesion scores in the IPG group rats were significantly lower compared to the CG group, the similar severity of fibrosis and local inflammation suggests that intra–abdominal administration of propolis may cause a local reaction by inducing a foreign body effect in the abdominal cavity.

Biochemical findings

When compared with the HCG group, it was noted that MDA levels increased in the abrasion–induced CG group, while GSH levels and CAT, GSH–Px and SOD activities decreased (P<0.05). In the SG group without abrasion, values for these parameters were found to be similar to those of CG group; MDA level being higher and GSH levels and CAT, GSH–Px and SOD activities lower than HCG group (P<0.05).

When the OPG group was compared with the HCG group, it was observed that all the parameters examined approached the HCG group means. When the IPG group was compared with the HCG group, it was noted that MDA levels were increased and SOD activities decreased than the HCG group averages(P<0.05), while GSH levels and CAT, GSH–Px activities approached the HCG group averages.

When compared with the CG group in which abrasion was created, it was observed that parameters, except GSH–Px, were statistically different from those for both OPG and IPG groups, with MDA was higher, while GSH, CAT and SOD were lower. According to the results obtained, it can be said that the recovery in the group where propolis was administered orally was more effective than the intra–abdominal application. It is seen that the recovery in the IPG group where intra–abdominal application was made was remarkably higher compared to the CG group. (TABLE IV).

TABLE IV
Statistical analysis of oxidative stress and antioxidant levels

Groups	MDA (nmol·mL^{-1})	GSH (µmol·mL^{-1})	CAT (k·g^{-1} Hb)	GSH–Px (U·mg^{-1} Hb)	SOD (U·g^{-1} Hb)
CG	9.74 ± 0.13^{c}	38.32 ± 0.94^{b}	39.61 ± 0.36^{b}	139.05 ± 2.36^{b}	56.37 ± 1.61^{c}
SG	9.45 ± 0.19^{c}	39.52 ± 0.55^{b}	39.94 ± 0.49^{b}	139.72 ± 2.17^{b}	56.79 ± 1.07^{c}
OPG	7.59 ± 0.17^{ab}	42.24 ± 0.43^{a}	47.81 ± 0.67^{a}	161.88 ± 5.38^{a}	72.33 ± 1.14^{ab}
IPG	8.09 ± 0.20^{b}	43.62 ± 0.41^{a}	42.58 ± 0.58^{a}	151.89 ± 1.75^{ab}	70.90 ± 0.75^{b}
HCG	7.06 ± 0.18^{a}	42.19 ± 0.78^{a}	49.47 ± 0.79^{a}	163.57 ± 3.98^{a}	76.15 ± 1.03^{a}
P	<0.001	<0.05	<0.001	<0.001	<0.001

In the study, the groups were defined as Control Group :(CG), Sham Group :(SG), Oral Propolis Group :(OPG), Intra–abdominal Propolis Group :(IPG) and Healthy Control Group :(HCG), significance (*P*). A lipid peroxidation marker: (MDA), Reduced Glutathione: (GSH), activity of Catalase: (CAT) and the Superoxide Dismutase: (SOD) and Glutathione Peroxidase activity (GSH–Px)

Diken Allahverdi *et al.* [34], in a study conducted to investigate the effectiveness of alpha–lipoic acid on intra–abdominal adhesions, reported that the tissue samples taken from the adhesion sites of rats treated with alpha–lipoic acid had lower MDA levels and higher GSH levels compared to the control group, and that these differences were statistically significant.

In the study conducted by Birben *et al.* [14], which investigated the effectiveness of intra–abdominal and oral propolis administration on intra–abdominal adhesions, it was observed that the level of MDA, an indicator of oxidative stress, was significantly lower compared to the control group, while antioxidant capacity indicators such as GSH, GSH–Px, CAT, and SOD were significantly higher.

Furthermore, the oxidative stress parameters of the rats in the OPG group showing values closer to those of the HCG group may be attributed to the foreign body effect caused by intra–

abdominal administration of propolis, leading to local reactions and/or peritoneal irritation.

CONCLUSION

As a result, according to the obtained data, it was determined that oral and intra–abdominal applications of water–based extract of propolis, which contains anti–inflammatory and antioxidant compounds, prevented the formation of intra–abdominal adhesions.

At the same time, when compared with the CG and SG groups, it was seen that the serum oxidative stress parameters of the rats in the OPG and IPG groups were almost at the same level as the HCG rats.

This study suggested that propolis could be used prophylactically to prevent adhesion formation after abdominal operations, either orally or intra–abdominal. In addition, with this study, it was concluded that it is very important to conduct studies on the therapeutic use of propolis, which is thought to be used for prophylactic purposes in intra–abdominal adhesions.

Conflicts of Interest

The authors of this article declare that there are no conflicts of interest.

Author Contributions

Conceptualization of the study: EP and DSS; Project implementation: EP, DSS, IC, and BC; Macroscopic Adhesion Score Analysis and Histopathological analyses: OO and MPO; Biochemical analyses: EK; Statistical analysis: EP; Manuscript writing: EP and DSS.

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BIBLIOGRAPHIC REFERENCES

[1] Kiliç N. The effect of *Aloe vera* gel on experimentally induced peritoneal adhesions in rats. Revue Méd. Vét. [Internet]. 2005 [cited July 21, 2025]; 156(7):409–413. Available in :https://goo.su/YWt4eik

[2] Arung W, Meurisse M, Detry O. Pathophysiology and prevention of postoperative peritoneal adhesions. World J. Gastroenterol. [Internet]. 2011; 17(41):4545–4553. doi: https://doi.org/bthgrq

[3] Schnüriger B, Barmparas G, Branco BC, Lustenberger T, Inaba K, Demetriades D. Prevention of postoperative peritoneal adhesions: A review of the literature. Am. J. Surg. [Internet]. 2011; 201:111–121. doi: https://doi.org/db96kb

[4] Köm M. Tavşanlarda Postoperatif İntraabdominal Adezyonların Önlenmesinde Hyaluronik asit/Karboksimetilselüloz Bariyerlerin Etkinliği [The efficacy of hyaluronic acid/carboxymethylcellulose barriers on the prevention of postoperative ıntraabdominal adhesions in rabbits]. FÜ Sağ. Bil. Vet. Derg. [Internet]. 2015 [cited May 22, 2025]; 29(2):75–79. Turkish. Available in: https://goo.su/NLtAQrj

[5] Kiyakli E, Köm M, Eröksüz Y, Baydar E. Ratlarda İntraabdominal Adezyonların Önlenmesinde Karboksimetilselüloz, Meloksikam ve Vitamin E Kombinasyonlarının Etkisi [Effect of combinations of carboxymethycellulose, Meloxicam and vitamin E on preventing ıntraabdominal adhesions in rats]. FÜ Sağ. Bil. Vet. Derg. [Internet]. 2017 [cited May 22, 2025]; 31(3):205–212. Turkish. Available in: https://goo.su/pupzx

[6] Sağliyan A, Aydin HB, Günay C, Durmus AS, Ceribasi S, Polat E. Fluniksin Meglumin ve Amniyon Sıvısının İntraabdominal Adezyonların Önlenmesi Üzerine Etkileri [The effects of Flunixin Meglumine and amnion fluid on the prevention of intraabdominal adhesions]. Erciyes Üniv. Vet. Fak. Derg. [Internet]. 2021; 18(2):75–83. Turkish. doi: https://doi.org/gkqqrb

[7] Köm M, Akay I, Polat E, Calik I. Ratlarda İntrabdominal Adezyonların Üzerine Trombositten Zengin Plazma'nın Etkisi [Effect of platelet rich plasma on ıntraabdominal adhesions in rats]. Van Vet. J. [Internet]. 2024; 35(1):1–6. Turkish. doi: https://doi.org/qgct

[8] Deynez G. Deneysel intra–abdominal adezyon modelinde etkili olabilecek tıbbi bitkiler üzerinde farmakognozik araştırmalar [Pharmacognosic evaluation of medicinal plants that can be effective against surgically–induced intra–abdominal adhesion model]. [dissertation on the Internet]. Ankara (Türkiye): University of Gazi; 2024 [cited May 6, 2025]. 173 p. Turkish. Available in: https://goo.su/LCP0l

[9] Günay C, Sağliyan A, Yaman İ. Ratlarda Deneysel Olarak Oluşturulan İntraabdominal Adezyonların Önlenmesinde Aprotinin İle Metilen Mavisinin Etkinliğinin Karşılaştırılması [Effects of aprotinin and methylene blue in prevention of experimentally performed intraabdominal adhesions in rats]. FÜ Sağlik Bil. Derg. [Internet]. 2005 [cited May 15, 2025]; 19(1):51–55. Turkish. Available in: https://goo.su/grMn6q

[10] Kabalar RB, Şahin ST, Ayhan S. Effect of intra–abdominal boric acid in the experimental adhesion model. Ulus Travma Acil. Cerrahi. Derg. [Internet]. 2024; 30(4):236–241. doi: https://doi.org/qgcv

[11] Arslan E. Sıçanlarda oluşturulan deneysel peritoneal adezyon modelinde Seprafilm ve Lovastatin'in karşılaştırılması [Comparison of lovastatin and seprafilm on experimental created peritoneal adhesion model in rats]. [thesis of specialization on the Internet]. Kayseri (Türkiye): University of Erciyes; 2009 [cited May 8, 2025]. 72 p. Turkish. Available in: https://goo.su/YNHD

[12] Havsteen BH. The biochemistry and medical significance of the flavonoids. Pharmacol. Therapeutics [Internet]. 2002; 96(2–3):67–202. doi: https://doi.org/fk38j8

[13] Ünal M, Öztürk O, Selcuk MY, Oruç MA. Propolis – Literatür Ne Diyor? [Propolis – What does the literature say?] Bozok Med J. [Internet]. 2020 [cited May 15, 2025]; 10(2):215–223. Turkish. Available in: https://goo.su/9zonY

[14] Birben B. Postoperatif Adezyonları Önlemede İntraperitoneal Propolis Tedavisinin Etkisi [The effect of propolis treatment to prevent postoperative intraperitoneal adhesions]. [thesis of specialization on the Internet]. Ankara (Türkiye): Başkent Üniversitesi; 2014 [cited May 9, 2025]. 71 p. Turkish. Available in: https://goo.su/bzahEc

[15] Yücel B, Topal E, Akçiçek E, Kösoğlu M. Propolisin İnsan Sağlığına Etkileri [Effects of propolis on human health]. Anadolu. J. AARI. [Internet]. 2014 [cited May 13, 2025]; 24(2):41–49. Turkish. Available in: https://goo.su/BpYqzya

[16] Miyataka H, Nishiki M, Matsumoto H, Fujimoto T, Matsuka M, Satoh T. Evaluation of propolis. I. Evaluation of Brazilian and Chinese propolis by enzymatic and physico–chemical methods. Biol. Pharm. Bull. [Internet]. 1997; 20(5):496–501. doi: https://doi.org/fgz3nc

[17] Marquele FD, DI Mambro VM, Georgetti SR,Casagrande R, Valim YM, Fonseca MJ. Assessment of the antioxidant activities of Brazilian extracts of propolis alone and in topical pharmaceutical formulations. J. Pharm. Biomed. Anal. [Internet]. 2005; 39(3–4):455–462. doi: https://doi.org/c2wdmr

[18] Celik S, Gorur S, Aslantas O, Erdogan S, Ocak S, Hakverdi S. Caffeic acid phenethyl ester suppresses oxidative stress in Escherichia coli–induced pyelonephritis in rats. Mol. Cell. Biochem. [Internet]. 2007; 297:131–138. doi: https://doi.org/ck9n32

[19] Song YS, Park EH, Hur GM, Ryu YS, Lee YS, Lee JY, Kim YM, Jin C. Caffeic acid phenethyl ester inhibits nitric oxide synthase gene expression and enzyme activity. Cancer Lett. [Internet]. 2002; 175:53–61. doi: https://doi.org/c8gw29

[20] Cikman O, Bulut A, Taysi S. Protective effect of propolis in protecting against radiation-induced oxidative stress in the liver as a distant organ. Sci. Rep. [Internet]. 2024; 14:21766. doi: https://doi.org/qgcw

[21] Askari VR, Rahimi VB, Zamani P, Fereydouni N, Rahmanian–Devin P, Sahebkar AH, Rakhshandeh H. Evaluation of the effects of Iranian propolis on the severity of post operational–induced peritoneal adhesion in rats. Biomed. Pharmacother. [Internet]. 2018; 99:346–353. doi: https://doi.org/gc7xx6

[22] Nair SK, Bhat IK, Aurora AR. Role of proteolytic enzymes in the prevention of postoperative intraabdominal adhesions. Arch. Surg. [Internet]. 1974; 108(6):849–853. doi: https://doi.org/fpf8nj

[23] Celepli S, Kismet K, Kaptanoğlu B,Erel S, Ozer S, Celepli P, Kaygusuz G, Devrim E, Gencay O, Sorkun K, Durak I, Akkuş MA.The effect of oral honey and pollen on postoperative intraabdominal adhesions. Turk. J. Gastroenterol. [Internet]. 2011; 22(1):65–72 .doi: https://doi.org/qgcx

[24] Placer ZA, Cushman L, Johnson BC. Estimation of products of lipid peroxidation in biological fluids. Anal. Biochem. [Internet]. 1966; 16:359–364. doi: https://doi.org/b96rpj

[25] Ellman GL, Courtney KD, Andres V, Featherstone RM. A new and rapid colorimetric determination of acetylcholinesterase activity. Biochem. Pharmacol. [Internet]. 1961; 7:88–95. doi: https://doi.org/fwdkkz

[26] Aebi H. Catalase *in vitro*. Methods Enzymol. [Internet]. 1984; 105:121–126. doi: https://doi.org/dnf7v9

[27] Beutler E. Red cell metabolism. A manual of biochemical methods. 2nd ed. New York (USA): Grune and Starton; 1984. 160 p.

[28] Sun Y, Oberly LW, Ying LA. Simple method for clinical assay of superoxide dismutase. Clin. Chem. [Internet]. 1988; 34(3):497–500. Available in: https://goo.su/Y6UMm

[29] Frankel S, Reitman S, Sonnen AC. A textbook on laboratory procedure and their interpretation. In: Gradwohl RBH, editor. Gradwohl's Clinical Laboratory Methods and Diagnosis. St. Louis (USA): The CV Mosby Company; 1970. 403–404 p.

[30] Sumbuloglu K, Sumbuloglu V. Biostatistics. 19th. ed. Ankara (Türkiye): Hatiboglu Yayinevi. 2019; p. 100–179.

[31] Kraemer B, Wallwiener C, Rajab TK,Brochhausen C, Wallwiener M, Rothmund R. Standardised models for inducing experimental peritoneal adhesions in female rats. BioMed. Res. Int. [Internet]. 2014; 435056:1–8. doi: https://doi.org/gb9knh

[32] Nian H, Pu Z, Li Z, Zhong P, Ma S, Li J. Establishment and evaluation of a stable and reliable rat model of peritoneal adhesions. Surgery [Internet]. 2024; 176(4):1256–1262. doi: https://doi.org/qgcz

[33] Gümüşgerdanli AC. Ratlarda Sistemik Rapamisin Uygulamasının Postoperatif Peritoneal Adezyonlar Üzerine Etkisi [Effects of systemic rapamycine administration on postoperative peritoneal adhesions in rats]. [thesis of specialization on the Internet]. Izmir (Türkiye): University of Dokuz Eylul; 2011 [cited May 10, 2025]. 50 p. Turkish. Available in: https://goo.su/Mpoc

[34] Diken Allahverdi T, Allahverdi E, Yayla S,Deprem T, Merhan O, Vural S, Sülü B, Günerhan Y, Köksal N. Effects of alpha lipoic acid on intra–abdominal adhesion: an experimental study in a rat model. Ulus Travma Acil. Cerrahi. Derg. [Internet]. 2015; 21(1):9–14.doi: https://doi.org/f7cf8q