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RESEARCH ARTICLE

The Comparison of the Effects of Platelet Rich Plasma and Streptokinase on Intra-Abdominal Adhesion: In the Rat Cecum Model

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ABSTRACT

This study aimed to investigate the effects of platelet rich plasma (PRP) and streptokinase (SK) on postoperative intra-abdominal adhesion formation in rats. The 4-month-old, healthy, non-pregnant female Wistar-Albino rats were used as animal material. The remaining 24 animals were divided into three groups with 8 rats in each group (PRP, SK and Control). The fibroblast proliferation, mononuclear cell infiltration and giant cells were clearly prominent in control group. A decrease was observed in the ratio of these cells in the PRP and SK groups. The comparison of the expression levels of *vWF*, *CASP3* and *IL-6* genes showed that the *vWF* gene was downregulated in the SK group and the *IL-6* gene was downregulated in the PRP and SK groups. They were statistically significantly compared to the control group. It was concluded that the expression level of *CASP3* gene decreased in the PRP and SK groups compared to the control group, but this decrease was not statistically significant. The PRP and SK could be applied intraperitoneal to prevent the adhesions after intra-abdominal surgery.

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INTRODUCTION

Adhesion formation is a complex process and defined as adhesion of intra-abdominal organs to one another or to the abdominal wall with fibrous bands. The cellular, biochemical and immunological factors take role in formation (Soltany, 2021). The abdominal surgery, peritoneal infections, chemotherapy, foreign body or abdominal tumors are reported as general reasons of adhesion (Scott *et al.,* 2021; Sudirman *et al.,* 2022). The traumatic damage of the mesothelial cells during abdominal surgery brings the connective tissues into contact with the peritoneal fluid. After this contact tissue plasminogen activity (PAA) decreases in the peritoneal fluid and leukotriene B_4 and prostaglandin E_2 levels increase. Depending on these changes fibrin starts to the adhesion formation, while repairs injured tissues. The decrease of PAA activity in the healing of peritoneal defects causes inhibition of fibrinolytic activity. The leukocytes and tissue plasminifibrinous peritoneal origin enzyme is insufficient to dissolve exudate by this way. Thus advancing of the fibrinous adhesion turns into a fibrin mesh and shapes the adhesion bands. As a result of the migration of fibrocyte and collagen deposition, the fibrin mesh grows and turns into permanent fibrous adhesions with the regression of capillaries and the filling of the area by fibroblasts. Despite advanced surgical techniques and medical treatment postoperative abdominal adhesion formation has not been completely prevented yet (Kocaay *et al.,* 2015; Çakır *et al.,* 2020; Van Steensel *et al.,* 2021; Wang *et al.,* 2023; Zhoa *et al.,* 2024).

Platelet-rich plasma (PRP) is a blood product used in wound healing, bone and cartilage regeneration, and maxillofacial surgery in human medicine (Man *et al.,* 2001; Cruciani *et al.,* 2024; Wang *et al.,* 2024). In the wound healing process the PRP accelerates the activation of platelets, increases the release of growth factors via stimulating the activation of platelets, and contributes to the formation of the building material and vascular network (Patel *et al.,* 2023). The main aim of the use of PRP is to stimulate cellular proliferation, regeneration and differentiation via to increase of releasing growth factors and cytokines from platelets, and to activate the collagen, hyaluronic acid productions, epidermal cell growth, and angiogenesis (Kobayashi *et al.,* 2020).

Streptokinase (SK), which converts plasminogen to plasmin, is a pharmacological agent that is thought to be effective in preventing peritoneal adhesions. It increases fibrinolysis and thus destroys fibrin residues (Yagmurlu *et al.,* 2003; Elgazzar *et al.,* 2022). Since SK can show its effect by directly binding to plasminogen, it does not have different enzymatic activity from urokinase and tissue plasminogen activators. SK is cheaper than other plasminogen-converting agents and extensively used in preventing adhesion formation. It is reported that the use of SK 100,000 IU/Kg dose as a fibrinolytic can prevent adhesion (Hosseini *et al.,* 2018; Varma *et al.,* 2020). However, it has an important disadvantage due to cause severe allergic reactions (Kunamnei *et al.,* 2007).

Von Willebrand Factor (*vWF*) has been reported as a blood glycoprotein which plays an important role in mediating platelet adhesion with the damaged site in the arterial circulation (Hoylaerts *et al.,* 1997; Zeineddin *et al.,* 2021; Wang *et al.,* 2024). High *vWF* levels are reported to be related with arterial thrombosis and the platelet-*vWF* interaction acts as a bridge between collagen and platelets, and plays an active role in adhesion formation (Lisman *et al.,* 2006; Barnes *et al.,* 2006; Mojzisch and Brehm, 2021; Wang *et al.,* 2024). A pro-inflammatory cytokine *interleukin-6* (*IL-6*) has a potential effect on various processes related to angiogenesis, fibrinolysis, and adhesion by stimulating the acute phase inflammation reaction (Ambler *et al.,* 2012; Gul *et al.,* 2022; Keret *et al.,* 2024). It has been reported that *CASP3*, which is one of the effector caspases plays a role in the adhesion mechanism by activating cell *adhesion molecule-1 (VCAM-1)* (Wang and Zhu, 2019).

The aim of this study was to investigate the effects of PRP and SK on postoperative intra-abdominal adhesion formation and to the effects of *vWF*, *IL-6* and *CASP3* at the level of histopathological, immunohistochemical and gene expression.

MATERIALS AND METHODS

The present study was completed in Erciyes University Experimental Research Application and Research Center (DEKAM) with the permission of Erciyes University Animal Experiments Local Ethics Committee (HADYEK, Decision no: 21/10).

The animal material of the study consisted of 32 healthy, 4-month-old, non-pregnant female Wistar-Albino rats with 150-200g. body weight. While 8 of these 32 animals included in the study were used as donors to obtain PRP, the remaining 24 animals were divided into three groups with 8 rats in each group: The adhesion control group, which did not undergo any intervention after the operation; the PRP group, in which PRP was applied after the operation, and the SK group, which was applied SK postoperatively.

After the preoperative preparation 10mg/kg xylazine HCL and 60mg/kg ketamine HCL were combinated in the same syringe and done intraperitoneally for general anesthesia. The skin incision was made dorsoventrally than abdominal tissues dissected very carefully to enter peritoneal cavity. Approximately a 2x2 cm^2 part of the antimesenteric dorsal surface of the cecum, which was taken out from the incision line, was brushed until punctate hemorrhage was formed. At the end of the brushing process, the abdominal regions of the animals in the control group were routinely closed without any application. The brushing area of the animals in the PRP group, PRP which obtained by modification of the method used by Stratakis *et al.* (2022) was sprayed to cover the defect intraperitoneally and the abdomen was closed. SK (2cc, 100,000U/kg, Sigma Aldrich, USA) was applied to the animals in the SK group by spraying it on the brushing area and the abdomen was closed.

Ketoprofen (0.04cc) was administered once subcutaneously as a postoperative analgesic to all operated animals. After the operation no nutrition program or diet was used for animals, and were followed for 14 days postoperatively. At the end of the period all animals were euthanized by decapitation method under general anesthesia.

Histopathological Evaluation: The obtained tissue samples (Adhesions bands, cecum) from groups were fixed in 10% formalin solution for 24 hours. The fixed tissues were washed in tap water than they were dehydrated by passing through graded alcohol series. After cleaning of tissues sample with xylol, they were embedded in paraffin than 5µm thick sections were taken from paraffin blocks. The sections were stained with Hematoxylin & Eosin (HE) and Masson Trichrome (MT) than visualized under an Olympus BX51 (Japan) light microscope for histopathologically evaluation (Balcıoğlu *et al.,* 2023). The adhesion, fibrosis and inflammation were evaluated in the obtained preparations by using Nair's (1974) scoring system (Table 1).

Table 1: Scoring system for adhesion, fibrosis and inflammation.

Adhesion	0.	No adhesion
	1.	Presence of only one adhesion band between the organs or between the organ and the abdominal wall
	2.	Presence of two bands between the organs or between the organs and the abdominal wall
	3.	Presence of more than two bands between the organs or between the organs and the abdominal wall, or mass formation of all intestines without adhesion to the abdominal wall
	4.	Adherence of an organ to the abdominal wall, regardless of the number and extent of adhesion bands
Fibrosis	0.	No fibrosis
	1.	Presence of minimal fibrosis
	2.	Presence of severe fibrosis
	3.	Presence of advanced fibrosis
Inflammation	0.	No inflammation
	1.	Giant cell plasma cell, lymphocyte
	2.	Giant cell, plasma cell, eosinophil, neutrophil
	3.	Numerous inflammatory cells, microabscesses

Immunohistochemistry: Immunohistochemistry staining method was used according to avidin-biotinperoxidase method based on the recommendations of the manufacturer. The 5µm thick sections were paraffinized in xylene and then rehydrated by passing through decreasing alcohol series. For antigen retrieval, it was boiled in citrate buffer solution (pH:6) in the microwave (750W) for 10 minutes and then kept at room temperature for about 20 minutes to cool.

Table 2: Primer sequences used in RT-qPCR analysis .

Gen	F (5'-3')	R (5'-3')
vWF	GCCTCTACCAGTGAGGTTTTGAAG	ATCTCATCTCTTCTCTTCTGCTCCAGC
CASP 3	AATTCAAGGGACGGGTCATG	GCTTGTGCGCGTACAGTTTC
IL-6	GACTTCCAGCCAGTTGCCTT	AAGTCTCCTCTCCGGACTTGT
GAPDH	GCAAGAGAGAGGCCCTCAG	TGTGAGGGAGATGCTCAGTG
HPRT1	TGTTTGTGTCATCAGCGAAAGTG	ATTCAACTTGCCGCTGTCTTTTA

After phosphate buffered saline (PBS) solution wash of the sections for 3x5 minutes, Ultra V Block Solution was applied for 5 minutes and incubated at 4ºC overnight with Caspase-3 primary antibody (9661s), anti vWF primer antibody (ab9378) and IL-6 (bs-0782R). Following the application of the primary antibody, biotinylated secondary antibody was applied for 10 minutes to the sections washed with PBS for 3x5 minutes. The sections washed with PBS for 3x5 minutes were incubated with peroxidase conjugated streptavidin for 10 minutes in a humid environment at room temperature and then taken into PBS. Immunohistochemical reactions were visualized with chromogen (diaminobenzidine tetra hydrochloride, DAB) (TH-125-HL). The tissues, which were counterstained with Mayer's hematoxylin, were passed through distilled water, dehydrated with graded alcohol series, passed through xylene and closed with an appropriate closure solution. Each preparation prepared by immunohistochemical staining method was examined and visualized under a light microscope (Olympus BX51, Tokyo, Japan) at 40X magnification. Ten different microscopic fields were evaluated for each sample and the number of CASP3 positive cells were counted. vWF and IL-6 immunoreactivity intensities were determined using Image J software.

RNA Isolation and c-DNA Synthesis: RNA was isolated from cecum samples with trizol (TriPureTrizol, Sigma, Cat. No. 11 667 157 001). DNAse (Invitrogen, Cat No: AM1906) was applied to the isolated RNA samples. RNA purity and concentration were measured with a nanodrop (Synergy H1Hybrid Multi-Mode Microplate Reader, BioTek, USA). c-DNA synthesis (Roche Ltd., Mannheim, Germany, Cat No: 04379012001) was performed using RNA.

Expression Analysis: The expression analysis was performed by a Light Cycler device (Roche Ltd., Mannheim, Germany), and by SYBR Green kit (Roche Ltd., Mannheim, Germany, Cat. No: 4673484001). This analysis was performed in double repeat and checked by melting curve analysis for non-specific binding. Ct values in the investigated genes were normalized with internal control genes (Table 2). These Ct values were suitable for statistical analysis by applying the $2^{-\Delta\Delta Ct}$ formula.

Statistical Analyses: IBM SPSS Statistics 21.0 for Windows (USA) program was used for statistical analysis. Descriptive statistics were presented as numbers and percentages for categorical variables and as mean, standard deviation, minimum and maximum for numerical variables. Comparisons of numerical variables among independent groups were performed with one-way ANOVA for normally distributed variables and with Kruskal Wallis test for non-normally distributed parameters. Differences between the ratios of categorical variables in independent groups were tested with Chi-Square and Fisher's exact test. Two-way analysis of variance (ANOVA) test was used in repeated measurements to examine the variation between groups.

RESULTS

The study and control groups' animals completed the protocol without any death during the experiment. In this process, no deterioration and infection in the wound area or intra-abdominal infection were observed. When the abdominal wall was opened, a difference was observed between the groups regarding the size of the adhesion bands. The adhesion bands in the control group were found to be quite distinct. In addition, it was observed that the cecum had extending bands both within itself and towards other organs and peritoneum. The adhesion bands had leaf or thin thread-like morphology in PRP and SK groups, and the formation in both groups was milder compared to the control group (Fig. 1). It was identified that the damage to the cecum surface was repaired macroscopically in all groups.

Statistical comparison of the adhesion bands between the groups pointed to no significant difference between control, PRP and SK groups based on Nair scoring. However, it was observed that the Nair score for adhesion partially decreased in the PRP and SK groups. The microscopic examination of the obtained images showed that although the amount of fibrosis and inflammation decreased in PRP and SK groups, this decrease did not lead to a difference between the groups (Table 3).

Table 3: Comparison of adhesion, inflammation and fibrosis between groups.

	Control group	PRP group	SK group	*p*
Adhesion	2.25±0.70	1.50±0.53	1.87±0.83	0.12
Inflammation	2.00±0.75	1.37±1.06	1.87±0.64	0.30
Fibrosis	1.87±0.83	1.62±0.74	1.62±0.74	0.66

Evaluation of H&E (Fig. 2) and MT (Fig. 3) stainings preparations of the groups showed that the mucosa and muscle layers could be clearly distinguished, but the parts of the serosa layer that were in contact with the adhesion region could not be distinguished and edema occurred in the serosa layer. In addition, it was determined that the adhesion bands were distributed from the serosa layer to the muscle and submucosa layer. It was found that edema occurred in the submucosa, especially around the vessel, and atrophy was present in the muscle layer, although it was more pronounced in the control group. The amount of atrophy and edema was less in the PRP group compared to the control group. There were dense focal areas of adipose tissue in the adhesion bands in the control group. It was observed that collagen fibers were dominant especially on the serosal surface and in the region where it was attached to the muscle layer. A decrease was observed in both focal adipose tissue and collagen fiber

amount due to treatment in the PRP and SK groups. Neovascularization was observed in all groups in the region where the adhesion bands were distributed from the serosa layer to the muscle and submucosa layer although it was more severe in the control group (Fig. 2&3). When the blood vessel numbers of the groups were compared, it was found that there was a significant difference between the control group and the PRP group (*p=0.04*) (Table 4).

Table 4: Comparison of vessel number, IL-6, vWF and caspase 3 reactions between groups.

	Control group	PRP group	SK group	*p*
Vessel number	2.98±1.83[a]	1.95±1.29[b]	2.42±1.60[ab]	0.040
IL-6	124.94±13.91[a]	86.73±4.91[b]	89.29±7.19[ab]	0.000
vWF	115.88±23.39[a]	99.11±21.36[b]	110.02±19.77[a]	0.000
CASP3	5.35±0.17[a]	8.38±0.09[b'']	7.93±0.07[ab]	0.023

The same letters on the same line a, b indicate the similarity between the groups, and different letters a, b indicate the difference.

Areas of inflammation, fibroblast proliferation, mononuclear cell infiltration and giant cells were clearly distinguished when the preparations belonging to the control group were evaluated at high magnification. A decrease was observed in the ratio of cells in the PRP and SK groups (Fig. 4).

Ten different areas from the sections taken from the tissues of 8 animals in each group were included in the measurement. While *IL-6* and *vWF* mean immunoreactivity intensities were calculated for all groups, apoptotic positive cells were counted in all groups stained with *CASP3* antibody and evaluated using the "Image J software" program at X40 and the results were recorded (Table 4). Analysis of the data obtained as a result of staining using *IL-6* primary antibody showed only a significant difference between the control group and the PRP group (*p=0.00*) (Fig. 4, Table 4). Examination of the data obtained as a result of staining using *vWF* primary antibody pointed to a significant difference between the PRP group and both the control group and the SK group (*p*=0.00). The number of apoptotic cells was evaluated with *CASP3*, which plays a key role in the demonstration of apoptotic cell death in the adhesion tissue. Examination of the data obtained as a result of staining using *CASP3* primary antibody demonstrated a significant difference between the control group and the PRP group (*p*=0.023).

RT-qPCR Results: Examination of the expression levels of *vWF, CASP3* and *IL-6* genes between groups showed that the expression level of the *vWF* gene was downregulated in the SK group, and the expression level of the *IL-6* gene was downregulated in the PRP and SK groups statistically significantly compared to the control group (*p*=0.00). It was concluded that the expression level of *CASP3* gene decreased in the PRP and SK groups compared to the control group, but this decrease was not statistically significant (Fig. 5).

DISCUSSION

Abdominal adhesions are one of the most important complications encountered in abdominal surgery due to cause high postoperative morbidity and mortality (Gill *et al.,* 2012). Hence, the studies about investigating on to prevent intra-abdominal adhesions always attract the attention of researchers (Stratakis *et al.,* 2022; Zhao *et al.,* 2024) This study aimed to investigate the relationship between the gene and protein expression levels of *vWF, CASP3* and *IL-6* and adhesion formation in rats that were postoperatively administered an autologous agent, PRP, and a fibronolytic agent, SK.

Different methods are preferred to create experimentally intra-abdominal adhesions in intra-abdominal organs (Lalountas *et al.,* 2010; Makarska *et al.,* 2010). In the study, the dorsal side of the antimesenteric part of the cecum body was traumatized with a tooth brush until petechial hemorrhages occurred to ensure adhesion formation. After the application, adhesion created in all traumatized animals. It showed that this application method was successful for adhesion formation.

Fig. 1: Macroscopic view of the adhesion bands (Yellow arrowhead) for the groups.

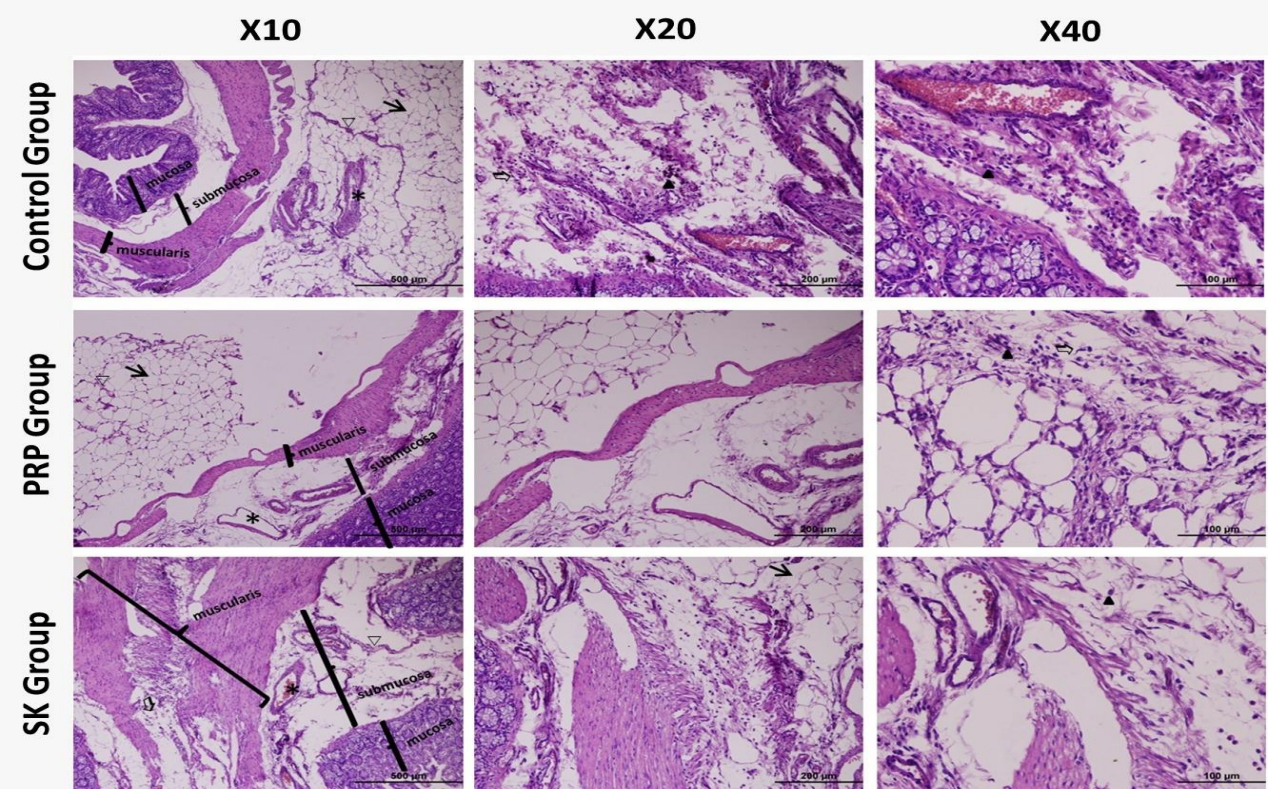

Fig. 2: View from the light microscope for the control and experimental groups (H&E), X10,20,40). Thin **arrow:** focal adipose tissue, ***:** blood vessel, ▽**:** adhesion band, ⇦**:**fibroblast proliferation, ▼**:**mononuclear cell infiltration, **Layers of the cecum wall**; mucosa, submucosa, muscularis.

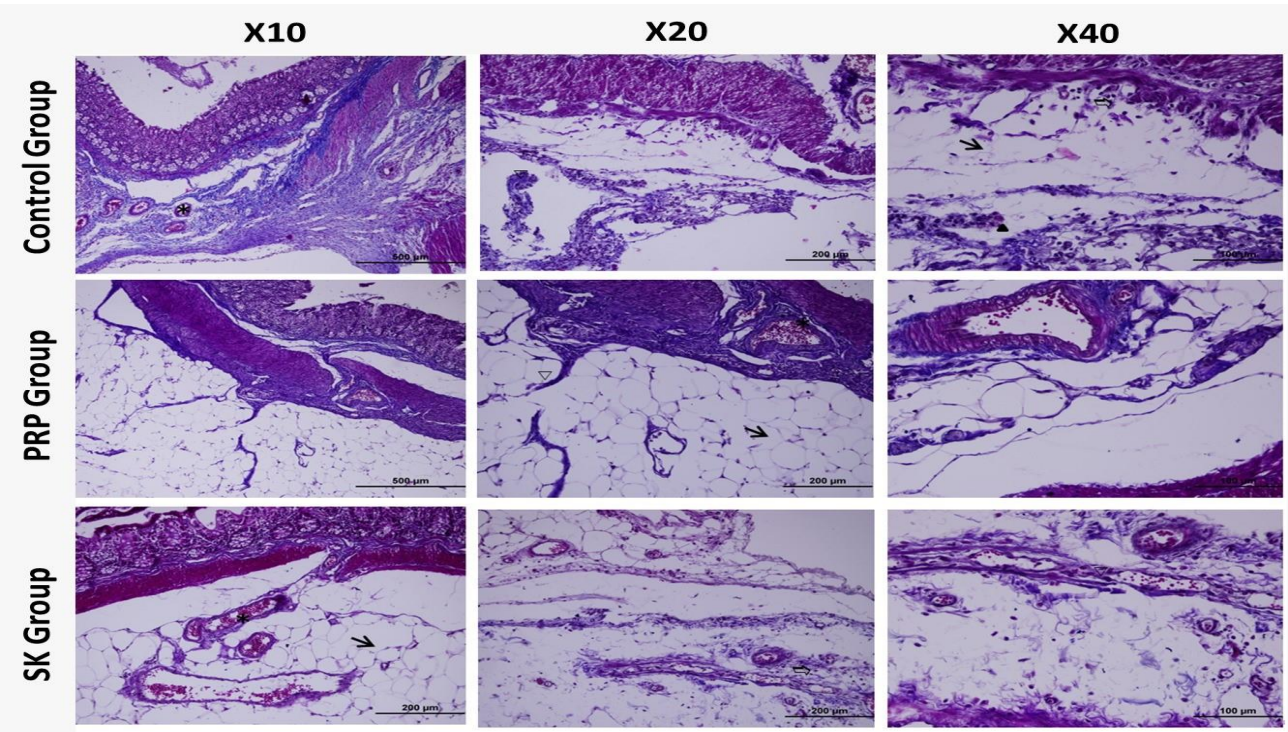

Fig. 3: View from the light microscope for the control and experimental groups (MT), X10,20,40).**Thin arrow:** focal adipose tissue, ***:** blood vessel, ▽**:** adhesion band, ⇦**:**fibroblast proliferation, ▼**:**mononuclear cell infiltration, **Layers of the cecum wall**; mucosa, submucosa, muscularis.

Intra-abdominal adhesion formation is a complex process involving cellular, inflammatory mediators and cytokines (Wei *et al.*, 2016). Cytokine release and oxidative stress are regarded as the first step of the adhesion formation mechanism (Arung *et al.*, 2011; Ward and Panitch, 2011). Interleukins, a member of the cytokine family, increase the adhesion formation by decreasing the fibrinolytic capacity of the tissue (Lucas *et al.*, 1996; Saba *et al.*, 1996). Studies on IL-6, which considers being a determinant of the inflammatory

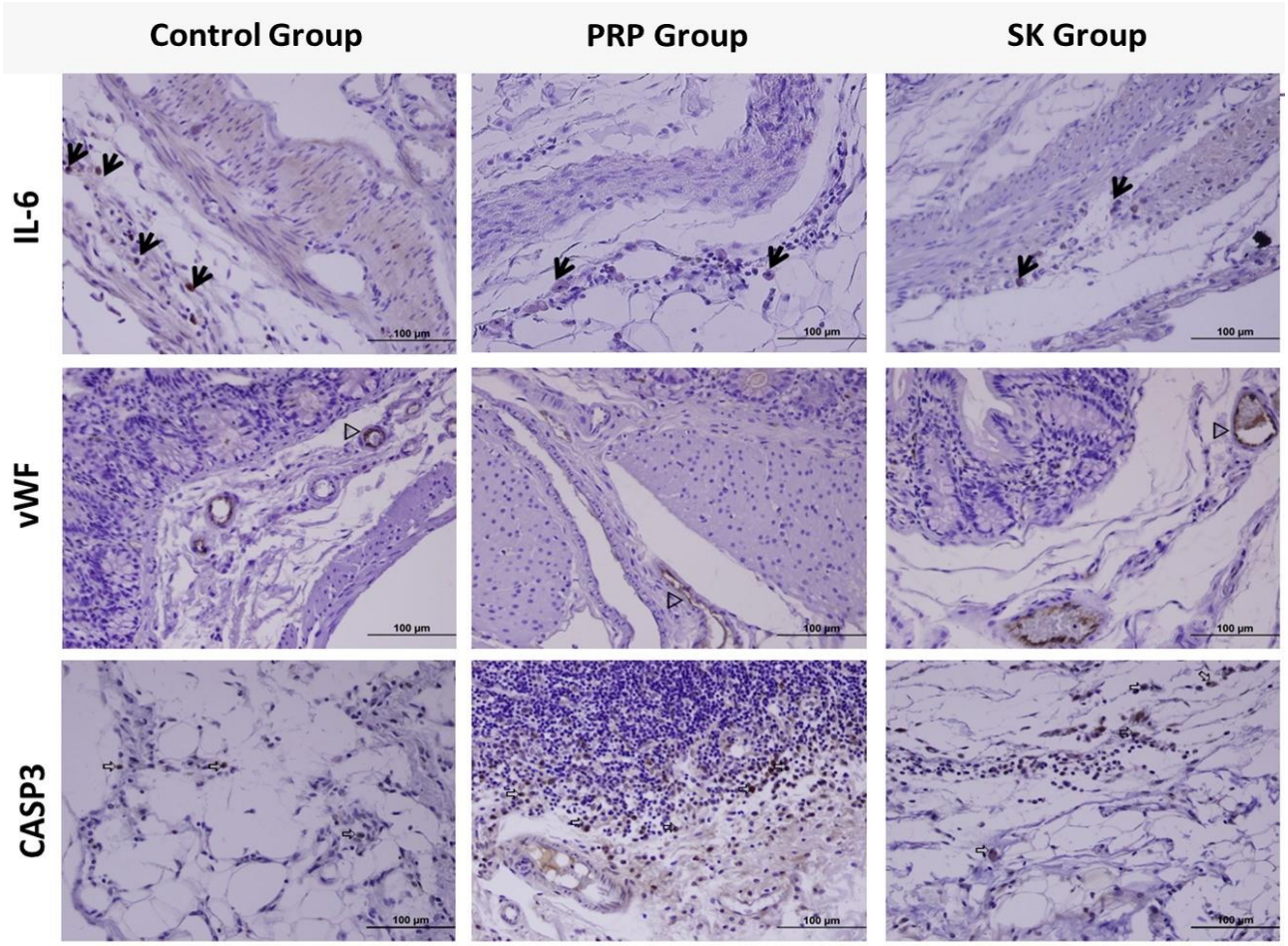

Fig. 4: IL-6, vWF and CASP3 expression in the adhesion sections of the control and experimental groups (X40). **Thin arrow:** IL-6 positive cell, **arrowhead:** vWF positive cell, **thick arrow:** CASP3 positive cell.

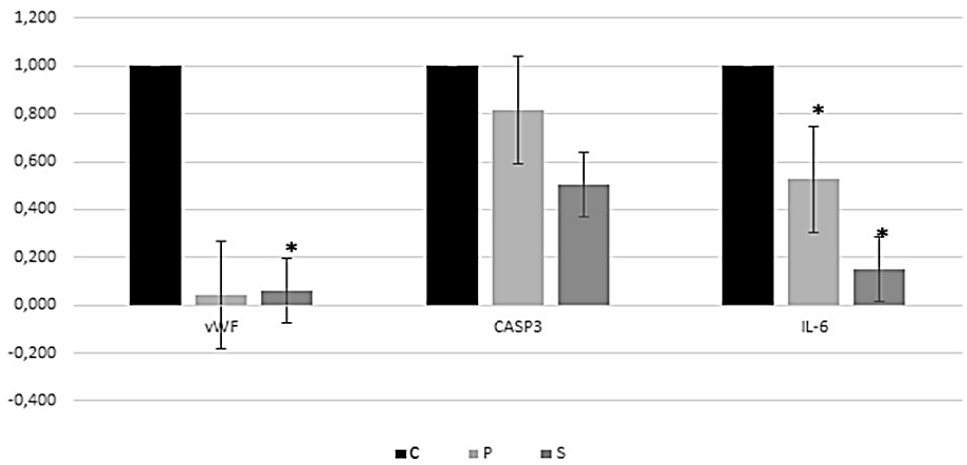

Fig. 5: Gene expression profiles between groups.
*$p<0.05$. C: Control group, P: PRP group, S: SK group

response and an important cytokine in adhesion formation, show that it is involved in the regulation of inflammatory and regenerative processes (Hassanabad *et al.*, 2021). After surgery *IL-6* level increases in traumatic area due to the various mechanisms has been reported (Imudia *et al.*, 2008; Ditzel *et al.*, 2012). It has been shown that fibroblast cell cultures made with cells taken from adhesion tissues have more *IL-6* than fibroblast cell cultures obtained from normal tissues (Ambler *et al.*, 2012). On the other hand, it was reported that intraperitoneal administration of breviscapine, which is effective in preventing postoperative adhesion formation, reduces blood serum *IL-6* level in rats (Zhang *et al.*, 2016). Hassanabad *et al.* (2021) reported that high *IL-6* plays a role in adhesion formation. Similarly, Uyama *et al.* (2019) reported that neutrophil leukocyte accumulation and adhesion formation decreased in animals at the end of monoclonal antibody treatment using *anti-IL-6* receptor in mice.

The present study concluded that the expression level of *IL-6* gene significantly decreased in the PRP group compared to the control group. Immunohistochemical findings also supported genetic findings, and it was concluded that at the end of the study that PRP had a suppressive effect on intra-abdominal adhesion formation.

Conditions such as insufficient perfusion in the tissues that contain adhesions reduce the chance of success to prevent the formation of intraperitoneal adhesions (Van Steensel *et al.,* 2021) On the other hand, the use of local agents has been highlighted in terms of both ease of application and the aim of showing the effect of the applied agent directly on the region in the prevention of intra-abdominal adhesion formation. For this reason, the use of local agents has become increasingly common in the prevention of adhesion formation instead of using systemic agents (Wang *et al.,* 2023; Zhao *et al.,* 2024).

SK is one of the fibrinolytic agents used in the prevention of abdominal adhesions. SK increases fibrinolysis via converting plasminogen to plasmin, which plays a key role in the mechanism of peritoneal adhesion formation, and thus plays an active role in the prevention of peritoneal adhesion formation by taking part in the destruction of fibrin residues (Dunn and Mohler, 1993; Kunamnei *et al.,* 2007).

Investigating the effectiveness of SK using on the development of intra-abdominal adhesion, Hosseini *et al.* (2018) found that 100,000 IU/kg SK administration in rats reduced the development of intra-abdominal adhesions by 50% due to the fibrinolytic effect of SK applied directly to the defected area. Smaniotto *et al.* (1997) applied SK at different doses intra-abdominally in created intra-abdominal adhesion model in rats, and observed adhesion in all groups after the application. However, at the end of the histopathological analysis of the tissue samples, they found that thinner and weaker adhesion bands formed in the groups in which SK was applied. They reported that 60,000IU/kg SK was applied group had less and weaker adhesion compared to the control group and 30,000 IU/kg SK applied group. On the other hand, they reported that the route of administration had no effect on the development of adhesion, and no difference was recorded comparing of same doses which were applied intravenous and spray in operation area. Jafari-Sabet *et al.* (2015) reported that SK reduced the development of intra-abdominal adhesion in mice due to its fibrinolytic effect.

In the present study, parallel to the literature, inflammation and fibrosis were detected in the histopathological analysis in SK group which performed 100,000U/kg SK to the wound area. Unlike other studies, this study demonstrated a statistically significant decrease in *IL-6* gene expression level in the SK group, and histopathological finding supported this condition. Both the data of this study and other studies showed that direct SK application in the wound area reduced the development of intra-abdominal adhesion.

Von Willebrand factor, a multimeric glycoprotein playing an important role in initiating the adhesion of platelets to the extracellular matrix, especially to collagen, has a concentration in circulation that increases rapidly in response to pathological stimuli, especially in the case of inflammation (Chegini, 2002; Barnes *et al.,* 2006; Springer, 2014; Bryckaert *et al.,* 2015; Keret *et al.,* 2024). High *vWF* level is also associated with arterial thrombosis, and the platelet-*vWF* interaction plays an active role in adhesion formation by acting as a bridge between collagen and platelets (Barnes *et al.,* 2001; Lisman *et al.,* 2006). In this study it was observed that the number of adhesive cells in the PRP group significantly decreased compared to the control group, and in parallel with the histopathological finding, the level of *vWF* gene expression in the PRP group was downregulated compared to the control group. The gene and protein expression of *vWF* decreased in the presence of PRP which might be due to platelet cells that are densely present in PRP. In the present study, the using *vWF* primary antibody, it was found that the number of adhesive cells decreased in the SK group compared to the control group, and the expression level of the *vWF* gene significantly decreased in the SK group compared to the control. This result is seen consistently with the literature. In addition, it is thought that SK application to the wound area reduces the *vWF* gene expression level in the wound region, thereby reducing the formation of intra-abdominal adhesions.

There may be a positive correlation between the increase in the level of *CASP3* (Lee *et al.,* 2014), protein, which is a protein effective on cell adhesion development, and adhesion/fibrosis after surgery (Kabalci *et al.,* 2020). This study identified a statistically significant difference between the *CASP3* protein level in the PRP group and the *CASP3* protein level in the control group as a result of the immunohistochemical analysis using *CASP3* antibody. It was seen that *CASP3* gene expression level was downregulated in the PRP group compared to the control group, supported the protein data. The increase in the number of apoptotic cells in the PRP group compared to the control group may have generated a decrease in the expression level of the *CASP3* gene, and it was demonstrated that the PRP application had an effect on the formation of intra-abdominal adhesions by decreasing the *CASP3* gene expression level.

Conclusion: The investigation of the adhesion formation is difficult due to it has a dynamic and complex process that can be induced by any peritoneal injury and it involves cellular, biochemical, immunological and biomechanical factors. Abdominal adhesion models, which are widely used by researchers, do not fully reflect the pathological mechanism of adhesion that may occur as a result of intra-abdominal surgery. In addition, the current understanding of the mechanism underlying abdominal adhesions has not been fully comprehended yet. Therefore, it is of critical importance to prevent the pathological mechanism of adhesion formation and to better understand the treatment modalities. This study concluded that PRP and SK could be applied directly to the wound area to prevent the formation of intra-abdominal adhesions after intra-abdominal surgery, and that these applications could contribute to preventing or reducing the formation of intra-abdominal adhesions.

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analysis, writing-original draft preparation, F D; investigation, data curation, K A; writing-original draft preparation, formal analysis, Y D; investigation, data curation, writing, B A; funding acquisition, formal analysis, supervision, validation.

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