Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 3 (5) April 2014: 40-45

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD
Global Impact Factor 0.533
Universal Impact Factor 0.9804

ORIGINAL ARTICLE

Fibrinolytic effects of *Matricaria chamomila* in preventing peritoneal adhesions

Minoo Rajaei[1], Aida Najafian[1], Soghra Fallahi*[2], Iman Asadi [3], Morteza Salimi[4], Mohammad Esmaeil Shahrzad[4], Tasnim Eghbal Eftekhaari[2],Kambiz Amjadi Golpaygani[3]

1- Obstetrics and Gynecology Department, Shariati hospital, Infertility and Reproductive Health Research Center, Hormozgan University of medical sciences, Bandarabbas, Iran
2- PhD by Research student of Molecular Medicine, Research Center for Molecular Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
3- Hormozgan Veterinary Department, Bandar Abbas, Iran.
4- Student Research Committee, Hormozgan University of Medical Sciences (HUMS), Bandar Abbas, Iran.

Email**:** Fallahi.Leila@gmail.com

ABSTRACT

Abdominal wall surgeries usually result in a common consequence which is peritoneal adhesion. Matrica chamomilla (MC) is a remedial herb with anti-inflammatory biologically active compounds which are effective in prevention of post-surgical adhesions. In this prospective study, 50 female rats were divided into 5 groups which received normal saline, chamomile extracts of 100mg/kg 200mg/kg 400 mg/kg and a control group. Intra-peritoneal ketamine 30 mg/kgwas administered for anesthesia. After surgical preparation of the abdomen, several scratches were made in the peritoneum and the abdominal wall was closed. Repeated laparotomy was performed 2 weeks later, and the peritoneum was biopsied for histo-pathological examination and grading of the adhesions. Data were analyzed with SPSS 13. Analysis was done using student's t-test, chi square, Kruskal- Wallis and Mann- Whitney U tests. If the value of p≤ 0.05 the results were considered significant. The results show that adhesion, fibrosis, inflammation, and post-surgical vascularization was significantly less in chamomile group compared to rats receiving normal saline or the control group (p≤0.001). Chamomile has protective anti-inflammatory effects proved by significant restraining of the post-surgical adhesions. (Abstract truncated at 185 words)

Keywords*: peritoneum adhesions; Matricaria Chamomila; Rat; fibrinolytic agents*

Received 20/02/2014 Accepted 19/03/2014

INTRODUCTION

Peritoneal adhesions are fibrous bands of tissue joining intra-abdominal organs to each other or to the abdominal wall [1, 2]. Adhesions are formed when the parietal or visceral peritoneum is damaged and the mesothelial layer basal membrane is exposed to surrounding tissues. The sequence of adhesion formation can be described as: 1- Tissue ischemia, 2- Inflammation, 3- Fibrin deposition, 4-Fibrin organization, 4-Collagen formation, and finally 5- maturation with the formation of adhesions [1,4]. Inflammatory mediators also may play an important role in adhesion formation [5]. Almost concurrently, migration of inflammatory cells, release of cytokines, and activation of the coagulation cascade results in an inflammatory response [6,7].The long-lasting approval of herbal medicines may be explained by the affinity of herbs to work gradually, usually with minimal toxic side effects. One of the most common herbs used for medicinal purposes is chamomile [8]. The common variation used for remedial purposes is Matricaria (MC). One of the medicinal plants that have been widely used is Matricaria Chamomile (MC) [9]. The flowering parts of chamomile can be used principally for an inflammatory condition [10]. Use of MC has been sustained by the segregation and documentation of several biologically active chemicals including polyphenols (flavonoids) and essential oil extracted from chamomile flowers [11]. MC containsterpenoids and azulenes (including chamazulene and enynedicolo ether) [12]. Anti-inflammatory properties ofterpenoids, bisabolol and chamazulenehave been well known [10]. Chamazulene strongly

suppresses the formation of leukotriene B4 in the neutrophile granulocytes [13],and also inhibits lipid peroxidation through antioxidant activity [14]. Furthermore, chamazulene inhibits peroxidation of arachidonic acid resulting reduced inflammatory mediators derived from arachidonic acid. A number of papers have been published on the identification of the phenolic compounds of MC includingapigenin, quercetin, and luteolin [15,16]. Some reports suggest that flavonoids have asignificantpart in inflammatory processes and immune functions by inhibiting several enzymes which are activated during certain inflammatory conditions [15]. For instance, luteolin, belonging to flavone (a subclass of flavonoids) has specific anti-inflammatory activities such as antioxidative enzymes activation, nuclear factor KappaB (NF-κB) pathway suppression, inhibition of pro-inflammatory substances, and reduction of the enhanced vascular permeability [17]. Apigenin, another flavone in the MC, that is non-toxic, non-mutagenic, and a potent antioxidant, effectively blocks intercellular adhesion molecule-1 up-regulation, leukocyte adhesion in response to cytokines, subdues cyclooxygenase-2 expression, and is a potential apoptosis inducer [18].Therefore, the effect of chamomile extract on the prevention of intra Peritoneal adhesions among rats was evaluated in this study.

MATERIALS AND METHODS

Animals and Anesthesia

Female Wistar rats (weighing 200-250g) taken from the central Animal House of Hormozgan University of Bandar Abbas, were used in this study. They were housed in environmentally controlled conditions (22±20 C, 12- hour light-dark cycle), with free access to standard pellet diet and water. Animals were kept in cages with raised floor to prevent coprophagy. After adaptation; the animals were randomly assigned to five different groups of equal numbers. The rats were prepared for surgery with an injection of ketamine (30mg/kg ip) for anesthesia. The surgical procedures were performed under sterile conditions.

Chemicals

The following chemicals were used: Extract of MC flowers Kashan (Iran). 0.9% NaCl (Serum Samen, Mashhad, Iran).

Induction of Adhesions

All of the animals were fasted for at least 12 hours immediately before surgery. After hair removal, the abdomen was cleaned with 1% antiseptic povidone- iodine solution and a 3 cm midline laparotomy was made, The peritoneal wall of the control group was completely stunned using sharp forceps and then the abdomen was sutured using nylon string 0.4. As for the normal group, 2 ml of Normal saline 0.9% was used for five minutes with IP after the manipulation then the abdomen was sutured. The other groups' abdomen was sutured after administering 100-200 mg of chamomile extract (400 mg/kg). All the surgeries were carried out by the same person under one single procedure. The animals' nutrition was controlled for two weeks.

Experimental Groups

Group 1 (Control group)
Group 2 (Normal Salin group)
Gourp 3 (*Matricaria chamomilla*100 mg/kg group)
Gourp 4 (*Matricaria chamomilla*200 mg/kg group)
Gourp 5 (*Matricaria chamomilla*400 mg/kg group)

Assessment of Adhesions

2 week after surgery, the animals were sacrificed. The abdominal cavity was shaved and opened via a 8 cm incision based in the lower abdomen for complete exploration. Blind evaluations were carried out; adhesions were graded from 0 (absent) to 4 (severe) according to the Mazujiclassification (19)(Table 1). In general, Grades 0 and 1 adhesions have no clinical significance, whereas Grades 3 and 4 adhesions can be a cause ofintestinal obstruction. Adhesion rate is used to describe the presence of an adhesion of any grade.After biopsy; the samples were fixed in formalin and sent to pathology lab for histology evaluations. The findings were compared with Adhesion Grading Classification.

Table 1- Adhesion grading according to Mazuji classification

Grade	Description of Grade
0	No adhesion
1	Very small, irregular adhesion
2	Easily separable medium intensity adhesion
3	Intense, not easily separable regular adhesion
4	Very intense, not easily separable, homogeneous adhesion

Histology

Histopathology examination was performed by two investigators. Adhesion-carrying tissues were excised en- block and fixed in a 10% buffered formaldehyde solution.Histologicalstudy was performed after

staining with hematoxylin and eosin. The evaluated parameters were fibrosis, inflammation, and vascular proliferation, rated on a modified semi-quantitative scale of 0-3(20-22). The amount of fibrosis was scored as follows: 0, no fibrosis; 1, minimal, loose fibrosis; 2, moderate fibrosis; and 3, florid dense fibrosis. Inflammation was scored as follows: 0: no inflammation; 1: presence of giant cell, occasional lymphocytes and plasma cell; 2: presence of giant cell, plasma cells, eosinophils and neutrophils; and, presence of many inflammatory cells and micro-abscesses. Vascular proliferation was scored as: 0: no vascular proliferation; 1: mild vascular proliferation; 2:moderate vascular proliferation; and 3: intense vascular proliferation.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for Social Science (SPSS 13). Differences in the numbers of animals without adhesions in the different treatment groups were evaluated using a Chi-square test. A t-test was used to determine differences between two independent populations.Kruskal-Wallis and Mann- Whitney U test were used if required. A value of $p \leq 0.05$ was considered significant.

RESULTS

Adhesion Grade and Rate

Throughout the investigation, severalanimals died during or after surgery. Adhesion rates and grades of the groups are presented in table 2. In comparing adhesion grades, a significant difference was found between the control group and the preventiongroups ($p = 0.004$).The more the dose of chamomile extract, the lesser the abdominal adhesion;administering chamomile extract with a dose of 200 mg/kg, adhesion was absent in90% of the cases and only 10% had (minimal) grade 1 adhesion.

Table 2- Postoperative adhesion rates, grades and side effects for groups Adhesion grade

Group	No. of rats	0	1	2	3	4	adhesion rate (%)	Side effects
(Control Group)	10	0	1	3	4	2	10/10(100)	Local hemtoma(n=3)
(Normal Saline Group)	10	1	0	2	3	0	6/10(60)	-
(MC100mg/kg Group)	10	4	4	1	1	0	6/10(60)	-
(MC200mg/kg Group)	10	6	3	1	0	0	4/10(40)	-
(MC400mg/kg Group)	10	9	1	0	0	0	1/10(10)	Local hemtoma(n=4)

1-

* $p \leq 0.05$ as compared to the control group and to the prevent groups (Group 3, 4 and 5) and with 2 group.

Adhesion rate is used to describe the presence of an adhesion in any grade.

On the other hand, in Group 5(MC400mg/kg Group) the adhesion grade differed significantly from that of the other groups ($p \leq 0.05$) (Table2). There were no adhesions in Grades 2 to 4 in the MC400mg/kg Group. Furthermore, most adhesion in the control, Normal SalineGroup (60%)was Grade 2 or 3 and MC400mg/kg Group were Grade 1 (10 %). Based on these findings, it was concluded that MC significantly reduced peritoneal adhesion development rate and adhesion grades. The adhesions in Group 5 (MC400mg/kg group) developed in the uncovered areas in the abdomen. But in groups 1 and 2(Control and Normal Saline) showed the highest incidence of postsurgical adhesion in comparisonof5groups ($p \leq 0.05$) (Table 4).

Table 3 – Histologic features of biopsies from adhesions (6, 7, and 28) Scores

Histologic Feature	0	1	2	3
Fibrosis				
Group 1	0	1	3	6
Group 2	0	0	2	4
Group 3	2	3	1	0
Group 4	3	1	1	0
Group 5*	0	1	0	0
Inflammation				
Group 1	0	4	2	4
Group 2	4	1	1	0
Group 3	5	1	0	0
Group 4	0	1	3	0
Group 5*	0	0	1	0
Vascular proliferation				
Group 1	3	2	3	2
Group 2	3	3	0	0
Group 3	2	4	0	0
Group 4	0	0	3	0
Group 5*	0	0	1	0

*p≤ 0.05 Compared to other groups(1.2,4, and 5)

Table 4 – Statistical comparison of the groups according to the adhesion grade

Groups	P-Value
Group 1 vs. Group 2	0.015
Group 1vs. Group 3	0.001
Group 1vs. Group4	0.000
Group 1vs. Group 5	0.000
Group 2vs. Group 3	> 0.05
Group 2vs. Group4	>0.05
Group 2vs. Group 5	0.052
Group 3vs. Group 4	> 0.05
Group 3vs. Group 5	> 0.05
Group 5vs. Group 4	> 0.05

Value of p≤ 0.05 was considered significant

Histology

The histologic findings of adhesion differed significantly among the Matricariachamomilla (MC) group and other groups according to fibrosis (p= 0.000), inflammation (p= 0.002), and vascular proliferation (p= 0.014). The (MC) group had a moderate score for fibrosis and the lowest scores for inflammation and vascular proliferation (Table 3). Histologic examination showed Groups1 and 2 had the the highest scores for fibrosis, inflammation and vascular proliferation. (Table 3)..

DISCUSSION

Postsurgical adhesion is a significant clinical problem for every surgical specialty. Evaluation of the causes and resources of inhibition of adhesion formation has been a major aimin many investigations. Several drugs and substances are used locally or systematically for this purpose, including mechanical barriers and physical, chemical, and pharmacological agents [20,21, 23-31]. However, despite positive reports, none of these have been approved for a standard therapy of adhesions [20,21,23]. The findings suggest that adhesions following abdominal surgeries are affected by a complex of factors including inflammation. The inflammatory cells finally migrate to the affected region and leading to cytokine release and activation of clotting factors.It is suggested that inflammatory mediators may play an important role in adhesion formation. There is experimental evidence that certain mediators, such as transforming growth factor-B (TGF-B) and interleukins, decrease the fibrinolyticcapability of the peritoneum and increase the adhesion formation [5, 32-34]. Chamomile has a extensive usage and is highlyreputed among herbal medicines during the history due to its anti-inflammatory, analgesic, antimicrobial, antispasmodic and sedative properties(10, 11).Based on previous studies and our study, the main anti-inflammatory mechanism of MC is summarized in Table 1.Probablemechanisms describing the role of MC compounds in prevention postsurgical adhesion include prevention of NF-kB activation and suppression of iNOS and COX-2 gene expression via apigenin and luteolin. The next mechanism is the antioxidant activity and prevention of lipid peroxidation of arachidonic acid, which blocks production of inflammatory substances via apigenin, luteolin, and chamazulene. Moreover, mechanisms such as inhibition of XO, vasodilatation inhibitory, and induction of apoptosis might also be important in the expression of anti-inflammatory effect of MC in prevention postsurgical adhesion.This study suggests that chamomile extract plays an important role in reducing inflammation resulting from abdominal surgeries ($p<0.05$). Besides, no grade 3 or 4 adhesion was observed among groups 4 and 5 compared with the control groups, specifically when chamomile extract was used with a dose of 200 and 400m/kg ($p<0.05$). Most of the adhesion ,fibrosis, inflammation and increased vascular proliferation was observed in the control group. (Table 3).Nicholas et al, have shown that apigeininhas anti-inflammatory effects by inactivation of NF-κB pathway through suppression of p65 phosphorylation which in turn blocks the expression of pro-inflammatory cytokines, such as interleukin 1 and 6 (IL-1, 6) and tumor necrosis factor-alpha (TNF-α) in human monocytes [35]. This effect regulates prostaglandin (PG) and NO production and suppresses inflammation [36]. Luteolin has anti-inflammatory effects including activation of antioxidativeenzymes, suppression of the NF-κB pathway, andinhibition of pro-inflammatory substances. Luteolin, iseffective in decreasing inflammation through lesseningof enhanced vascular permeability [17]. It also subdues production of NO andProstaglandins 2 (PGE2) as well as the expression ofiNOS, cyclooxygenase-2 (COX-2), TNF-α and IL-6 viablocking NF-κB activation pathway [37].Histological findings of this study detect that chamomile extract could prevent adhesion. The results of group 5 specifically present this difference more completely compared with the control group.

CONCLUSION

It is noteworthy to state that this is a pioneer study and that the previous studies didn't consider this feature of chamomile. Therefore, further studies are required on different animal groups for reassurance

Table 1. Main anti-inflammatory mechanisms of MC.

Mechanism	Compound	Reference
Modulation of NF-Kb	Apigenin	Nicholas et al. [35]
	Luteolin	Chen et al. [37]
Vascular dilation inhibitor	Luteolin	Seelinger et al. [17]
LTB4 blocker	Chamazulene	Safayhi et al. [13]
Antioxidant activity	Apigenin	Lee et al. [18]
	Luteolin	Seelinger et al. [17]
	Chamazulene	Rekka et al. [14]
Suppresses gene expression of iNOS and COX-2	Apigenin	Nicholas et al. [35]
	Luteolin	Chen et al. [37]

ACKNOWLEDGMENTS

It should be noted that this study was a multicentre teamwork between Hormozgan University of Medical Sciences and Veterinary Office of the province as well. The authors of this article would like to hereby express their gratitude to Dr. ZabihollahGharib, the veterinarian Organization President for his support and assistance.

CONFLICT OF INTEREST

NONE

REFERENCES

1. Menzies D, Ellis H. (1990). Intestinal obstruction from adhesions--how big is the problem? Annals of the Royal College of Surgeons of England.;72(1):60.
2. Ellis H, Moran BJ, Thompson JN, Parker MC, Wilson MS, Menzies D, et al. (1999), Adhesion-related hospital readmissions after abdominal and pelvic surgery: a retrospective cohort study. The Lancet. 353(9163):1476-80.
3. Coleman M, McLain A. (2000). Impact of previous surgery on time taken for incision and division of adhesions during laparotomy. Diseases of the colon & rectum. 43(9):1297-9.
4. Milligan D, Raftery A. Observations on the pathogenesis of peritoneal adhesions: a light and electron microscopical study. British Journal of Surgery. 1974;61(4):274-80.
5. Tsukada K, Katoh H, Shiojima M, Suzuki T, Takenoshita S, Nagamachi Y. Concentrations of cytokines in peritoneal fluid after abdominal surgery. The European journal of surgery. 1993;159(9):475-9.
6. Holmdahl L, Ivarsson ML. The role of cytokines, coagulation, and fibrinolysis in peritoneal tissue repair. European Journal of Surgery. 1999;165(11):1012-9.
7. Reijnen M, Bleichrodt R, Van Goor H. Pathophysiology of intra-abdominal adhesion and abscess formation, and the effect of hyaluronan. British Journal of Surgery. 2003;90(5):533-41.
8. Astin JA, Pelletier KR, Marie A, Haskell WL. Complementary and Alternative Medicine Use Among Elderly Persons: One-Year Analysis. Journal of Genauology: MEDICAL SCIENCES. 2000;55(1):M4-M9.
9. Aside R, Khakpour S, Borzoie M, Mahmudi F, Fallahi S. Matricaria Chamomile: Prevention of Abdominal Adhesions. International Electronic Journal of Medicine. 2013;2(1):3-10.
10. Gardiner P. Complementary, Holistic, and Integrative Medicine Chamomile. Pediatrics in Review. 2007;28(4):e16-e8.
11. McKay DL, Blumberg JB. A review of the bioactivity and potential health benefits of chamomile tea (Matricaria recutita L.). Phytotherapy Research. 2006;20(7):519-30.
12. Ganzera M, Schneider P, Stuppner H. Inhibitory effects of the essential oil of chamomile (Matricaria recutita L.) and its major constituents on human cytochrome P450 enzymes. Life sciences. 2006;78(8):856-61.
13. Safayhi H, Sabieraj J, Sailer E-R, Ammon H. Chamazulene: an antioxidant-type inhibitor of leukotriene B4 formation. Planta medica. 2007;60(05):410-3.
14. Rekka EA, Kourounakis AP, Kourounakis PN. Investigation of the effect of chamazulene on lipid peroxidation and free radical processes. Research communications in molecular pathology and pharmacology. 1996;92(3):361.
15. Avallone R, Zanoli P, Puia G, Kleinschnitz M, Schreier P, Baraldi M. Pharmacological profile of apigenin, a flavonoid isolated from *Matricaria chamomilla*. Biochemical pharmacology. 2000;59(11):1387.

16. Švehlíková V, Bennett RN, Mellon FA, Needs PW, Piacente S, Kroon PA, et al. Isolation, identification and stability of acylated derivatives of apigenin 7-glucoside from chamomile (Chamomilla recutita [L.] Rauschert). Phytochemistry. 2004;65(16):2323-32.
17. Seelinger G, Merfort I, Schempp CM. Anti-oxidant, anti-inflammatory and anti-allergic activities of luteolin. Planta medica. 2008;74(14):1667-77
18. Lee J-H, Zhou HY, Cho SY, Kim YS, Lee YS, Jeong CS. Anti-inflammatory mechanisms of apigenin: inhibition of cyclooxygenase-2 expression, adhesion of monocytes to human umbilical vein endothelial cells, and expression of cellular adhesion molecules. Archives of pharmacal research. 2007;30(10):1318-27.
19. Mazuji M, KALAMBAHETI K, PAWAR B. Prevention of adhesions with polyvinylpyrrolidone: Preliminary report. Archives of surgery. 1964;89(6):1011.
20. Ersoy E, Ozturk V, Yazgan A, Ozdogan M, Gundogdu H. Comparison of the two types of bioresorbable barriers to prevent intra-abdominal adhesions in rats. Journal of Gastrointestinal Surgery. 2009;13(2):282-6.
21. Hooker GD, Taylor BM, Driman DK. Prevention of adhesion formation with use of sodium hyaluronate–based bioresorbable membrane in a rat model of ventral hernia repair with polypropylene mesh—A randomized, controlled study. Surgery. 1999;125(2):211-6.
22. Koçak I, Ünlü C, Akçan Y, Yakin K. Reduction of adhesion formation with cross-linked hyaluronic acid after peritoneal surgery in rats. Fertility and sterility. 1999;72(5):873-8.
23. Kaptanoglu L, Kucuk H, Yegenoglu A, Uzun H, Eser M, Mentes C, et al. Effects of seprafilm and heparin in combination on intra-abdominal adhesions. European Surgical Research. 2008;41(2):203-7.
24. Avsar AF, Avsar FM, Sahin M, Topaloglu S, Vatansev H, Belviranli M. Diphenhydramine and hyaluronic acid derivatives reduce adnexal adhesions and prevent tubal obstructions in rats. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2003;106(1):50-4.
25. Kesting MR, Loeffelbein DJ, Steinstraesser L, Muecke T, Demtroeder C, Sommerer F, et al. Cryopreserved Human Amniotic membrane for soft tissue repair in rats. Annals of plastic surgery. 2008;60(6):684-91
26. Corrales F, Corrales M, Schirmer CC. Preventing intraperitoneal adhesions with vitamin E and sodium hyaluronate/carboxymethylcellulose: a comparative study in rats. Acta Cirurgica Brasileira. 2008;23(1):36-41.
27. Sahin Y, Saglam A. Synergistic effects of carboxymethylcellulose and low molecular weight heparin in reducing adhesion formation in the rat uterine horn model. Acta obstetricia et gynecologica Scandinavica. 1994;73(1):70-3.
28. Türkçapar A, Ozarslan C, Erdem E, Bumin C, Erverdi N, Kutlay J. The effectiveness of low molecular weight heparin on adhesion formation in experimental rat model. International surgery. 1995;80(1):92.
29. Bulbuller N, Ilhan YS, Kirkil C, Cetiner M, Gogebakan Ö, Ilhan N. Can angiotensin converting enzyme inhibitors prevent postoperative adhesions? Journal of Surgical Research. 2005;125(1):94-7.
30. Kucuk HF, Kaptanoglu L, Kurt N, Uzun H, Eser M, Bingul S, et al. The role of simvastatin on postoperative peritoneal adhesion formation in an animal model. European Surgical Research. 2007;39(2):98-102.
31. Nair SK, Bhat IK, Aurora AL. Role of proteolytic enzyme in the prevention of postoperative intraperitoneal adhesions. Archives of surgery. 1974;108(6):849.
32. Ghellai AM, Stucchi AF, Chegini N, Ma C, Andry CD, Kaseta JM, et al. Role of transforming growth factor beta-l in peritonitis-induced adhesions. Journal of Gastrointestinal Surgery. 2000;4(3):316-23.
33. AL-JAYYOUSI RH, Medcalf JF, Harris KP. Role of transforming growth factor beta in peritoneal fibrosis. Nephrology. 2002;7(5):216-9.
34. Whawell S, Thompson J. Cytokine-induced release of plasminogen activator inhibitor-1 by human mesothelial cells. The European journal of surgery. 1995;161(5):315-8.
35. Nicholas C, Batra S, Vargo MA, Voss OH, Gavrilin MA, Wewers MD, et al. Apigenin blocks lipopolysaccharide-induced lethality in vivo and proinflammatory cytokines expression by inactivating NF-κB through the suppression of p65 phosphorylation. The Journal of Immunology. 2007;179(10):7121-7.
36. Ha SK, Lee P, Park JA, Oh HR, Lee SY, Park J-H, et al. Apigenin inhibits the production of NO and PGE< sub> 2</sub> in microglia and inhibits neuronal cell death in a middle cerebral artery occlusion-induced focal ischemia mice model. Neurochemistry international. 2008;52(4):878-86.
37. Chen C-Y, Peng W-H, Tsai K-D, Hsu S-L. Luteolin suppresses inflammation-associated gene expression by blocking NF-κB and AP-1 activation pathway in mouse alveolar macrophages. Life sciences. 2007;81(23-24):1602-14.

Citation of this article

Minoo R, Aida N, Soghra F, Iman A, Morteza S, Mohammad E S, Tasnim E E, Kambiz A G. Fibrinolytic effects of *Matricaria chamomila* in preventing peritoneal adhesions.Bull. Env. Pharmacol. Life Sci., Vol 3 (5) April 2014: 40-45