

Effect of *Rosa damascene* Mill. Hydroalcoholic Extract on the Treatment of Chronic Idiopathic Constipation in Adults

ARTICLE INFO

Article Type

Original Research

Authors

Sadeghi H.¹ PhD,
Alamdari M.² MD,
Hasanzadeh S.^{*2} MD,
Jokar S.² MD,
Panahi Kokhedan E.¹ PhD,
Malekzadeh J.³ PhD,
Abbasi R.⁴ PhD

How to cite this article

Sadeghi H, Alamdari M, Hasanzadeh S, Jokar S, Panahi Kokhedan E, Malekzadeh J, Abbasi R. Effect of *Rosa damascene* Mill. Hydroalcoholic Extract on the Treatment of Chronic Idiopathic Constipation in Adults. Journal of Clinical Care and Skills. 2021;2(1):29-34.

ABSTRACT

Aims Constipation is an important problem and dysfunction of the digestive system. In the traditional beliefs of different parts of the world, especially Iran, *Rosa damascene* Mill. has several properties, including sedative, anti-inflammatory, anti-seizure, anti-depressant, and laxative effects. This study aimed to evaluate the effect of hydroalcoholic extract of *Rosa damascene* Mill. in treating chronic constipation in adults.

Materials & Methods This randomized clinical trial was performed in 2018 in Shahid Mofteh Specialized Clinic of Yasouj on 160 patients with chronic constipation referred to internal medicine and gastroenterologists. Extracted hydroalcoholic extract of *Rosa damascene* Mill. and lactulose syrup was used; The control group received 20cc of lactulose syrup twice a day, and the intervention group received a hydroalcoholic extract of *Rosa damascene* Mill. two times a day in the form of 500mg capsules twice a day for one month. Data were analyzed using SPSS 19 software and T and chi-square tests with 95% confidence interval.

Findings During the intervention process, 16 people did not refer to the necessary follow-up, and the necessary information was collected from 144 patients with chronic constipation. Sixty-eight patients (4.2%) were male, and 76 (52.8%) were female. The mean age of patients was 43.18 ± 13.67 , and the age range was 18 to 75 years. There was no statistically significant difference between the two groups' mean age and sex under *Rosa damascene* Mill.'s intervention. Hydroalcoholic extract and lactulose ($p < 0.05$). Also, there was no statistically significant difference between the variables of frequency and ease of defecation between the two groups receiving lactulose and *Rosa damascene* Mill. hydroalcoholic extract before and after the intervention ($p < 0.05$).

Conclusion Hydroalcoholic extract of *Rosa damascene* Mill. has a similar effect to lactulose in the treatment of chronic constipation in adults.

Keywords Chronic Constipation; Hydroalcoholic Extract of *Rosa damascene* Mill.; Lactulose

¹Medicinal Plants Research Center, Yasuj University of Medical Sciences, Yasuj, Iran

²Internal Medicine Department, Faculty of Medicine, Yasuj University of Medical Sciences, Yasuj, Iran

³Nutrition Department, Faculty of Health Sciences, Yasuj University of Medical Sciences, Yasuj, Iran

⁴Pediatric Department, Faculty of Medicine, Yasuj University of Medical Sciences, Yasuj, Iran

*Correspondence

Address: Internal Medicine Department, Faculty of Medicine, Yasuj University of Medical Sciences, Yasuj, Iran.

Phone: -

Fax: +98 (74) 33220162

sajadhasanzadeh@yahoo.com

Article History

Received: July 30, 2019

Accepted: June 30, 2020

ePublished: February 01, 2021

CITATION LINKS

[1] Epidemiology of constipation in Europe and ... [2] A population-based study on bowel habits ... [3] Dietary fiber intake, dietary glycemic index and ... [4] Prevalence of gastrointestinal symptoms ... [5] Bowel habit reference values and ... [6] Chronic idiopathic ... [7] Constipation in children and young people ... [8] Functional chronic constipation: Rome ... [9] Essential oils and their therapeutic ... [10] The laxative and prokinetic effects of Rosa ... [11] Development and clinical evaluation of ... [12] Adverse effects ... [13] A study on the relationships between ... [14] Global value chain analysis of Damask ... [15] The effect of aromatherapy with ... [16] Induced anti-oxidation efficiency and ... [17] Interventions of Iranian traditional medicine ... [18] Ziziphus jujuba extract for the treatment ... [19] Validity and reliability of the Bristol Stool ... [20] Update on Rome IV criteria for colorectal ... [21] The constipation severity instrument ... [22] Pharmacological effects of Rosa ... [23] Analgesic and anti-inflammatory effects ... [24] Hepatoprotective effect of Stachys pilifera ... [25] A simple practice guide for dose ... [26] Laxative effects of Rosa damascene Mill ... [27] Chemical constituents, experimental and ... [28] An in vitro evaluation of various Rosa damascena ... [29] Effect of aqueous fraction of Rosa damascena ... [30] Effect of Rosa damascena Mill. flower ... [31] Comparative efficacy and safety of ... [32] Cochrane review: Lactulose versus ... [33] Polyethylene glycol 3350 without electrolytes ... [34] Lactitol or lactulose in the treatment ... [35] Relaxing effect of rose oil on ...

Introduction

Constipation is a common clinical disease and one of the important reasons for referring to family doctors and gastroenterologists, whose prevalence in western societies is reported to be up to 20% [1]. Studies in Asia have reported a prevalence of 16.5% in Korea and 26% in young women in Japan [2, 3]. In studies conducted in Iran, the prevalence of constipation has varied between 3.5% in Tabriz [4] to 32.9% [5] in Isfahan.

Etiologically, constipation may have congenital or acquired causes, and the most common congenital disease that causes constipation is Hirschsprung. Acquired causes of constipation include altered nutritional and behavioral patterns such as poor diet, low fiber, limited fluid intake, especially water, inactivity and obesity, medication, metabolic and endocrine, neurological and psychological disorders, as well as disorders Intestine-like tumors [6]. Diseases that cause constipation may be local or systemic [7]. Chronic constipation, according to Rome IV criteria [8], includes

- Straining during defecation in more than 25% of cases of defecation;
- Hard stools in more than 25% of cases of defecation;
- Feeling of incomplete bowel movements for more than 25% of cases of defecation;
- Feeling of anal obstruction in more than 25% of cases of defecation;
- Manual maneuver to facilitate defecation of more than 25% of feces (e.g., finger emptying);
- Less than three bowel movements per week;
- Excretion without laxatives is rare, and there are no diagnostic criteria for IBS (Irritable Bowel Syndrome).

Of course, according to the Rome IV diagnostic criteria, mild abdominal pain and some bloating may be present, but they are not prominent, and these symptoms should be present for at least three months in the last six months of the doctor's diagnosis.

There are several non-pharmacological and pharmacological treatments for constipation. Non-pharmacological therapies include recommendations to increase mobility (exercise), dietary recommendations, and lifestyle changes in general, some of which have not been proven [9]. Pharmacological treatments include disimpactions, bulking laxatives, osmotic laxatives, and stimulant laxatives [10-13]. Due to the effect of constipation on people's quality of life and dissatisfaction with common drugs, patients and researchers have tended to use other methods such as herbs and other methods of complementary and alternative medicine. One of the plants that the Iranians have used for a long time is *Rosa damascene* Mill. [14]. *Rosa damascene* Mill. is widely used in traditional Iranian medicine not only because of its effective therapeutic effects

but also because of its religious beliefs. This plant is used in traditional medicine to treat abdominal and chest pain, menstrual bleeding, and digestive problems [10, 15, 16]. In traditional medicine of Iran and some countries, *Rosa damascene* Mill. is used to treat constipation [17]. The gauge of hydroalcoholic extract of *Rosa damascene* Mill. has increased stool water volume and stool frequency in laboratory animals [10, 18]. Besides, some animal studies have reported that *Rosa damascene* Mill. decoction has also had strong laxative effects such as increasing stool volume and increasing the number of bowel movements [10]. Dried flowers of *Rosa damascene* Mill. are also available in the Iranian medicinal plants market, the powder of which is also used to treat constipation [17]. Considering the traditional application and results of animal studies on the beneficial effects of *Rosa damascene* Mill. in the treatment of constipation and the lack of clinical studies that have addressed the effect of *Rosa damascene* Mill. in the treatment of adult constipation, this study aimed to investigate the effect of hydroalcoholic extract of *Rosa damascene* Mill. in the treatment of constipation in chronic adult.

Materials & Methods

This randomized clinical trial was performed in 2018 in Shahid Mofteh specialized clinic affiliated to Yasouj University of Medical Sciences on patients with chronic constipation who had been referred to internal medicine and gastroenterologists. According to the predictable recovery percentage formulas with lactulose based on similar studies and predictable recovery percentage with *Rosa damascene* Mill. hydroalcoholic extract, the sample size of each group was determined between 73 people and considering 10% shedding; finally, 80 people in each group were considered. Using the available sampling method, 160 people eligible to participate in the study were selected based on their history and physical examination by an internal medicine specialist, and patients were randomly divided into two groups using quadruple blocks (block = 80). n). Only those who had chronic constipation according to Rome IV criteria (such as having two or more criteria) were included in the study; They did not have the underlying disease (hypothyroidism, diabetes, lead poisoning, celiac disease) and structural disease; They did not receive constipation treatments before the initial visit, and there was no blood in their stools (performing three stool tests for blood).

Data were collected by an internal medicine specialist using the Bristol Scale [19] and researcher-made checklists based on reliable sources. To evaluate the consistency of feces and follow the symptoms of constipation, the doctor used the Bristol scale, which was asked by looking at the photos of this scale and asking about fecal conditions [19]. The researcher-made checklist consisted of two sections: demographic information and stool frequency and

defecation classifications. In order to compare the severity of chronic constipation in terms of stool frequency before treatment, the following classification was used that patients were divided into one of these three groups:

- 3 times or more weekly with difficulty (in this group, the patient must have at least 2 Rome IV criteria for difficulty defecating)
- 2 times a week with difficulty (in this group, the patient must have at least one Rome IV criterion for difficulty defecating)
- Once a week with difficulty (in this group, the patient must have at least one Rome IV criterion for difficulty defecating)

In order to compare the severity of chronic constipation in terms of frequency of defecation after treatment, patients were divided into four fecal excretion groups:

- Three times a week without difficulty;
- Four times a week without difficulty;
- once a day without difficulty; and
- more than once a day without difficulty

Also, to compare the severity of chronic constipation in terms of comfort before treatment, patients were divided into three groups: having one criterion, having two criteria, and having three or more criteria of Rome IV indicators [20, 21]. To compare the severity of chronic constipation in terms of comfort after treatment classification, complete comfort, relative comfort, and inconvenience in fecal excretion were used.

This study was presented and approved by the Research Ethics Committee of Yasouj University of Medical Sciences and was registered in the clinical trial system. After explaining the study's objectives, informed consent was received from all participants before the start of the study. Participants were randomly assigned to one of the two intervention and control groups through a four-block random allocation, and this process continued until the sample size of 80 people in each group was completed. The information was confidential, and the patients' privacy was taken into consideration when completing the checklists.

In order to extract the *Rosa damascene* Mill. Furthermore, prepare the hydroalcoholic extract of the *Rosa damascene* Mill., some dried *Rosa damascene* Mill. was first prepared and approved by a herbalist. The petals were separated and washed and then mixed with 70% ethanol and placed in an incubator at 46-48°C for 48 hours. 200g of *Rosa damascene* Mill. powder was extracted each time the extract was made. The resulting mixture was filtered and concentrated by a rotary apparatus at 46°C under vacuum conditions in the next step. It was then placed in the freezer and prepared in the required dose when used in capsules [22-24]; The dose of *Rosa damascene* Mill. extract was selected based on the conversion of animal dose to human dose, as in a study in which the dose of 180-190mg/kg caused

laxative effects in dogs, and therefore this dose was converted to human dose [25, 26].

Lactulose syrup (Sobhan Company; Iran) was used as one of the standard treatments for constipation, along with *Rosa damascene* Mill. hydroalcoholic extract capsule. The intervention included administration of hydroalcoholic extract of *Rosa damascene* Mill. in the intervention group and lactulose administration in the control group. Outcome variables to be assessed included frequency of bowel movements, ease or difficulty of bowel movements, time of onset of *Rosa damascene* Mill. hydroalcoholic extract and lactulose, and their side effects. The control group received 20cc of lactulose syrup twice a day, and the intervention group received a hydroalcoholic extract of *Rosa damascene* Mill. 2 times a day in the form of 500mg capsules in 2 divided doses (2 times a day) for one month [27]. All subjects were followed up weekly by a fixed internal medicine specialist for one month to determine the symptoms of chronic constipation according to the Bristol scale and by asking patients after starting treatment, in addition to data on stool frequency, comfort, or difficulty in defecation, time of onset of effect of hydroalcoholic extract of *Rosa damascene* Mill. Furthermore, the doctor completed lactulose and their side effects up to one month per week. Physicians, statisticians, and patients were unaware of the individual belonging to each of the study groups.

SPSS 19 statistical software was used to analyze the data. Quantitative data such as age between the two groups were compared by independent T-test with a 95% confidence interval. The intragroup change was also compared with paired T-test. Wilcoxon test (marked rank) was used to compare before and after each group about the number of excretions and excretion status, which were not normal distribution and the data were qualitative. Comparison of sex ratio distribution between the two groups and excretion status was compared using the chi-square test.

Findings

During the intervention process, 16 people, including 10 in the control group and 6 in the intervention group, did not refer for the necessary follow-up, and the necessary information was collected from 144 patients with chronic constipation. Sixty-eight patients (47.2%) were male, and 76 (52.8%) were female, of which 35 (47.3%) males and 39 (52.7%) females were in *Rosa damascene* Mill. hydroalcoholic extract group and 33 (47.1%) males and 37 (52.9%) females were in the lactulose group. The mean age of patients was 43.18±13.67, and the age range was 18 to 75 years. There was no statistically significant difference between the two groups' mean age and sex under *Rosa damascene* Mill.'s intervention. hydroalcoholic extract and lactulose ($p>0.05$).

All patients had difficult bowel movements at the beginning of treatment and the number of bowel movements per week was low. The chi-square test results showed no statistically significant difference between the frequency of defecation with difficulty before the intervention between the two groups receiving lactulose and *Rosa damascene* Mill. hydroalcoholic extract ($p=0.76$; Table 1). After treatment and receiving lactulose and hydroalcoholic extract of *Rosa damascene* Mill., all patients had easy bowel movements, and no disease reported difficulty in bowel movements; More than 75.7% in the group consuming *Rosa damascene* Mill. hydroalcoholic extract had one or more bowel movements, and in the group receiving lactulose, about 55.7% had bowel movements more or less; However, the difference was not significant ($p=0.058$; Table 1).

Table 1) Absolute and relative frequency of variable stool frequency in the two groups receiving *Rosa damascene* Mill. hydroalcoholic extract and lactulose before and after the intervention (numbers in parentheses are percentages)

Fecal excretion	<i>Rosa damascene</i> Mill.	Lactulose	Total
Before Intervention			
3 times and more	31 (41.89)	33 (47.14)	64 (44.44)
2 times in week	34 (45.94)	28 (40.00)	62 (43.06)
1 time and lesser in week	9 (12.17)	9 (12.86)	18 (12.50)
Total	74 (100)	70 (100)	144 (100)
After Intervention			
3 times in week	4 (5.40)	7 (10.00)	11 (7.64)
4 times in week	14 (18.92)	24 (34.29)	38 (26.39)
1 time in day	39 (52.70)	31 (44.29)	70 (48.61)
1 time and more in day	17 (22.98)	8 (11.42)	25 (17.36)
Total	74 (100)	70 (100)	144 (100)

Before the intervention, no significant difference was found between the feeling of comfort in the excretion of the intervention and control groups ($p = 0.46$; Table 2). After the intervention, none of the recipients of the *Rosa damascene* Mill. felt uncomfortable, and 4.3% of the patients receiving lactulose still felt uncomfortable after consuming lactulose, but this difference was not significant ($p=0.17$; Table 2).

Table 2) Absolute and relative frequency of defecation variables in the two groups receiving *Rosa damascene* Mill. hydroalcoholic extract and lactulose before and after the intervention (numbers in parentheses are percentages)

Ease of defecation	<i>Rosa damascene</i> Mill.	Lactulose
Before Intervention		
1 criterion	22 (29.73)	21 (30.00)
2 criteria	39 (52.70)	44 (62.9)
3 criteria and more	13 (17.57)	5 (7.14)
After Intervention		
Complete comfort	40 (54.05)	39 (55.71)
Relative comfort	34 (45.95)	28 (40.00)
Lack of comfort	0	3 (4.29)

Although both drugs effectively treat chronic constipation in adults, the onset of therapeutic effects of *Rosa damascene* Mill. hydroalcoholic extract appeared faster. In all patients, with the consumption of *Rosa damascene* Mill. within 24-48 hours after the

start of treatment, a favorable therapeutic response was observed, and with the use of lactulose, within 48-72 hours after the start of treatment, a favorable therapeutic response was observed. No side effects were seen in any of the patients who received *Rosa damascene* Mill. extract, but in patients receiving lactulose, side effects such as nausea and vomiting, heartburn, and bloating were reported.

Discussion

In traditional medicine of Iran and some countries, *Rosa damascene* Mill. is traditionally used in the treatment of chronic constipation [28]. However, a review of published studies showed that no scientific or clinical studies had been found to confirm *Rosa damascene* Mill.'s effect. hydroalcoholic extract in the treatment of chronic constipation in adults. Therefore, this study was performed to evaluate the effect of the hydroalcoholic extract of *Rosa damascene* Mill in treating chronic constipation in adults.

The clinical results obtained from the present study showed that the hydroalcoholic extract of *Rosa damascene* Mill. at a dose of 1g (2 capsules of 500mg) per day, effectively treating chronic constipation in adults. Due to the lack of a study on the effectiveness of hydroalcoholic extract of *Rosa damascene* Mill. in humans, the results were further compared with animal studies. Dolati *et al.* showed that the hydroalcoholic extract of *Rosa damascene* Mill. was dose-dependently able to increase contraction in guinea pig ileum [29]. Abbaszadeh *et al.* also reported that the use of *Rosa damascene* Mill. hydroalcoholic extract in a dose-dependent manner caused diarrhea in dogs [26]. In the present study, in some participants, the frequency increased to 3 to 4 times. Kazerani *et al.* also showed that *Rosa damascene* Mill. decoction could cause prokinetic effects in rats [10]. Besides, Arzomand *et al.* conducted a study to determine the prokinetic and laxative effects of *Rosa damascene* Mill. on mice. In this study, the results showed that the hydroalcoholic extract of *Rosa damascene* Mill. increased the frequency of bowel movements, moisture, and stool volume compared to the placebo group. This study's proposed mechanism is to stimulate the osmotic infiltration of water into the intestine, which can be said that in humans, it can stimulate the osmotic infiltration of water into the intestine resulting in looser stools and easier defecation [10]. Another study investigated the effect of *Rosa damascene* Mill. on ileum rat in extrinsic conditions. In this study, it was noted that the contractile effect of *Rosa damascene* Mill. on ileum, the rat is more through acetylcholine-dependent pathways. However, the role of other excitatory neurotransmitters should also be considered. The study also found that phytochemically, *Rosa damascene* Mill. contains compounds such as tannins, gallic acid, malic acid, resins, and flavonoids,

including camphor and quercetin, but it is not possible to specify which of these components in the stimulatory effects of *Rosa damascene* Mill. on ileum is involved and needs further studies [30].

The results of the present study on lactulose are similar to the results of previous studies. Pich *et al.* showed that lactulose 3350 could relieve chronic constipation in adults and had no side effects in patients [31]. Lee *et al.* also showed that administration of lactulose 3350 in constipation treatment was able to relieve constipation in adults [32]. As the results of the present study, Loening-Baucke *et al.* both treatments had a long-term effect on constipation and showed that lactulose was safe in the one-year treatment of constipation and had better absorption than magnesium milk in children, although side effects such as bloating, nausea, and vomiting in lactulose has been reported [33].

Also, the frequency and ease of excretion with the treatment of hydroalcoholic extract of *Rosa damascene* Mill. at a dose of 1g (2 capsules of 500mg) per day was more than lactulose at a dose of 1g per kg of body weight per day. The number of patients who had defecation with hydroalcoholic extract of *Rosa damascene* Mill. more than once a day was 17 patients (23%); eight patients (11.4%) experienced lactation more than once a day. In terms of daily defecation without problems, both groups were almost the same.

The results showed no side effects in patients receiving *Rosa damascene* Mill. hydroalcoholic extract, but side effects such as nausea and vomiting, heartburn, and bloating were reported in lactulose recipients, although the side effects were so mild that no need to stop treatment or treat complications. The results regarding the side effects of lactulose in humans are contradictory, and some studies have not reported any side effects; While some studies indicate the occurrence of complications such as bloating, nausea, and vomiting [34]. One study mentioned that lactulose has less side effects such as bloating, nausea, and vomiting than *Rosa damascene* Mill. Furthermore, it has sedative, stress-reducing, and depressing properties [35].

The use of only one dose of *Rosa damascene* Mill. extract was the main limitation of this study. According to the present results, it is suggested that more similar research be done on the use of effective and pure *Rosa damascene* Mill. compounds to treat constipation in order to provide sufficient scientific evidence.

Conclusion

Hydroalcoholic extract of *Rosa damascene* Mill. has a similar effect to lactulose in the treatment of chronic constipation in adults.

Acknowledgments: We thank the Vice Chancellor for Research of Yasouj University of Medical Sciences and Medicinal Plants Research Center, the staff of the internal

ward of Imam Sajjad Hospital in Yasouj, as well as all those who have helped in the implementation of this project.

Ethical Permissions: This study has been proposed and approved by the ethics committee in the research of Yasouj University of Medical Sciences (ethics code: IR.YUMS.REC.1397.113). This study is also registered in the clinical trial system and has the clinical trial code IRCT20190124042481N1.

Conflicts of Interests: All authors declare that there are no conflicts of interests.

Authors' Contribution: Sadeghi H. (First Author), Writer of Introduction/Methodologist/Main Researcher/Statistical Analyst/Writer of Discussion (25%); Hassanzadeh S. (Second Author), Writer of Introduction/Methodologist/Main Researcher/Statistical Analyst/Writer of Discussion (20%); Alamdari M. (Third Author), Statistical Analyst (15%); Jokar S. (Fourth Author), Assistant Researcher (10%); Panahi Koukhdan I. (Fifth Author), Assistant Researcher (10%); Malekzadeh J.M. (Sixth Author), Assistant Researcher (10%); Abbasi R. (Seventh Author), Assistant Researcher (10%)

Funding/Sources: This project was supported by the Vice-Chancellor for Research of Yasouj University of Medical Sciences.

References

- 1- Peppas G, Alexiou VG, Mourtzoukou E, Falagas ME. Epidemiology of constipation in Europe and Oceania: A systematic review. *BMC Gastroenterol.* 2008;8:5.
- 2- Jun DW, Park HY, Lee OY, Lee HL, Yoon BC, Choi HS, et al. A population-based study on bowel habits in a Korean community: Prevalence of functional constipation and self-reported constipation. *Dig Dis Sci.* 2006;51(8):1471-7.
- 3- Murakami K, Sasaki S, Okubo H, Takahashi Y, Hosoi Y, Itabashi M. Dietary fiber intake, dietary glycemic index and load, and body mass index: A cross-sectional study of 3931 Japanese women aged 18-20 years. *Eur J Clin Nutr.* 2007;61(8):986-95.
- 4- Khoshbaten M, Hekmatdoost A, Ghasemi H, Entezariasl M. Prevalence of gastrointestinal symptoms and signs in northwestern Tabriz, Iran. *Indian J Gastroenterol.* 2004;23(5):168-70.
- 5- Adibi P, Behzad E, Pirzadeh S, Mohseni M. Bowel habit reference values and abnormalities in young Iranian healthy adults. *Dig Dis Sci.* 2007;52(8):1810-3.
- 6- Epstein D. Chronic idiopathic constipation. *Continu Med Educ.* 2009;27(5).
- 7- National Collaborating Centre for Women's and Children's Health (UK). Constipation in children and young people: Diagnosis and management of idiopathic childhood constipation in primary and secondary care. London: RCOG Press; 2010.
- 8- Russo M, Strisciuglio C, Scarpato E, Bruzzese D, Casertano M, Staiano A. Functional chronic constipation: Rome III criteria versus Rome IV criteria. *J Neurogastroenterol Motil.* 2019;25(1):123-8.
- 9- Momeni T, Shahrokhi N. Essential oils and their therapeutic actions. Tehran: University of Tehran Press; 1991. [Persian]
- 10- Arezoomandan R, Kazerani HR, Behnam-Rasooli M. The laxative and prokinetic effects of *Rosa damascena* Mill in rats. *Iran J Basic Med Sci.* 2011;14(1):9-16.
- 11- Sheikh ZA, Khan AA, Nawaz A, Zahoor A, Khan SS, Usmanghani K. Development and clinical evaluation of polyherbal laxative laxisen. *RADS J Pharm Pharm Sci.* 2014;2(2):63-70.

- 12- Xing JH, Soffer EE. Adverse effects of laxatives. *Dis Colon Rectum*. 2001;44(8):1201-9.
- 13- Nikbakht A, Kafi M. A study on the relationships between Iranian people and Damask rose (*Rosa damascena*) and its therapeutic and healing properties. *Acta Hort*. 2004;790:251-4.
- 14- Mohammadzadeh SH, Karim MH, Karbasi AR. Global value chain analysis of Damask Rose in the world and Iran. *The Second International Conference on Rosa damascena*. Mashhad: Ferdowsi University; 2019.
- 15- Amini A, Bahraminejad N, Jafari S, Kamali K. The effect of aromatherapy with *rosa damascena* essence on postoperative pain in inguinal hernia repair: A randomized clinical trial. *Nurs Midwifery Stud*. 2020;9(3):117-23.
- 16- Attia H, Al-Yasi H, Alamer K, Esmat F, Hassan F, Elshazly S, et al. Induced anti-oxidation efficiency and others by salt stress in *Rosa damascena* Miller. *Scientia Horticulturae*. 2020;274:109681.
- 17- Hashem Dabaghian F, Taghavi Shirazi M, Amini Behbahani F, Shojaei A. Interventions of Iranian traditional medicine for constipation during pregnancy. *J Med Plant*. 2015;14(53):58-68. [Persian]
- 18- Naftali T, Feingelernt H, Lesin Y, Rauchwarger A, Konikoff FM. *Ziziphus jujuba* extract for the treatment of chronic idiopathic constipation: A controlled clinical trial. *Digestion*. 2008;78(4):224-8.
- 19- Blake MR, Raker JM, Whelan K. Validity and reliability of the Bristol Stool Form Scale in healthy adults and patients with diarrhoea-predominant irritable bowel syndrome. *Aliment Pharmacol Ther*. 2016;44(7):693-703.
- 20- Simren M, Palsson OS, Whitehead WE. Update on Rome IV criteria for colorectal disorders: Implications for clinical practice. *Curr Gastroenterol Rep*. 2017;19(4):15.
- 21- Varma MG, Wang JY, Berian JR, Patterson TR, McCrea GL, Hart SL. The constipation severity instrument: A validated measure. *Dis Colon Rectum*. 2008;51(2):162-72.
- 22- Boskabady MH, Shafei MN, Saberi Z, Amini S. Pharmacological effects of *Rosa damascena*. *Iran J Basic Med Sci*. 2011;14(4):295.
- 23- Hajhashemi V, Ghannadi A, Hajiloo M. Analgesic and anti-inflammatory effects of *Rosa damascena* hydroalcoholic extract and its essential oil in animal models. *Iran J Pharm Res*. 2010;9(2):163-8.
- 24- Panahi Kokhdan E, Ahmadi K, Sadeghi H, Sadeghi H, Dadgary F, Danaei N, et al. Hepatoprotective effect of *Stachys pilifera* ethanol extract in carbon tetrachloride-induced hepatotoxicity in rats. *Pharm Biol*. 2017;55(1):1389-93.
- 25- Nair AB, Jacob S. A simple practice guide for dose conversion between animals and human. *J Basic Clin Pharm*. 2016;7(2):27-31.
- 26- Abbaszadeh M, Kazerani HR, Kamrani A. Laxative effects of *Rosa damascene* Mill in dogs. *J Appl Anim Res*. 2010;38(1):89-92.
- 27- Akram M, Riaz M, Munir N, Akhter N, Zafar S, Jabeen F, et al. Chemical constituents, experimental and clinical pharmacology of *Rosa damascena*: A literature review. *J Pharm Pharmacol*. 2020;72(2):161-74.
- 28- Tabrizi H, Mortazavi SA, Kamalinejad M. An in vitro evaluation of various *Rosa damascena* flower extracts as a natural antisolar agent. *Int J Cosmet Sci*. 2003;25(6):259-65.
- 29- Dolati K, Rakhshandeh H, Shafei MN. Effect of aqueous fraction of *Rosa damascena* on ileum contractile response of guinea pigs. *Avicenna j Phytomed*. 2013;3(3):248-53.
- 30- Sadraei H, Asghari G, Emami S. Effect of *Rosa damascena* Mill. flower extract on rat ileum. *Res Pharm Sci*. 2013;8(4):277-84.
- 31- Piche T, Dapoigny M. Comparative efficacy and safety of lactulose plus paraffin vs polyethylene glycol in functional constipation: A randomised clinical study. *United Eur Gastroenterol J*. 2020;8(8):923-32.
- 32- Lee-Robichaud H, Thomas K, Morgan J, Nelson RL. Cochrane review: Lactulose versus polyethylene glycol for chronic constipation. *Evid Based Child Health Cochrane Rev J*. 2011;6(3):824-64.
- 33- Chung S, Cheng A, Goldman RD. Polyethylene glycol 3350 without electrolytes for the treatment of functional constipation in infants and toddlers. *Can Fam Physician*. 2009;55(5):481-2.
- 34- Maydeo A. Lactitol or lactulose in the treatment of chronic constipation: Result of a systematic. *J Indian Med Assoc*. 2010;108(11):789-92.
- 35- Hongratanaworakit T. Relaxing effect of rose oil on humans. *Nat Prod Commun*. 2009;4(2):291-6.