Pharmacogn. Res., 2025; 17(3):867-872.
https://www.phcogres.com

Original Article

# *Fumaria parviflora* Lam. Aqueous Extract Versus Simethicone in the Treatment of Infantile Colic: A Prospective Randomized Clinical Trial

**Vahid Ramezani[1], Mahmood Noori Shadkam[2], Mobina Ghiasirad[3], Sayedeh Ebrahimi[3], Ali Mohammad Ranjbar[3,4,*]**

[1]Department of Pharmaceutics, Faculty of Pharmacy, Traditional Pharmacy and Pharmaceutical Sciences Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, IRAN.
[2]Department of Pediatrics and Mother and Newborn Health Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, IRAN.
[3]Department of Pharmacognosy, Faculty of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, IRAN.
[4]Department of Pharmacognosy, Traditional Pharmacy and Pharmaceutical Sciences Research Center, Faculty of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, IRAN.

## ABSTRACT

**Background:** infantile colic observes 10 to 40% of infants during first few months of life. **Objectives:** The purpose of the present study was to evaluate the effectiveness of *Fumaria parviflora* Lam. (will fumitory) aqueous extract on infantile colic. **Materials and Methods:** A total of 52 breastfed infants suffering from infantile colic were randomly assigned to two groups. Will fumitory group and simethicone group received will fumitory extract and simethicone for 10 days, respectively. During the period of study, changing in infants' colic symptoms including duration of crying, stooling frequency and consistency as well as probable side effects were inquired every day from the parents. **Results:** The reduction in daily crying duration (<50%) was significantly in will fumitory group (25 vs. 6; $p<0.001$) as well as cure rate of 100% in this group. There were no significant differences in weight gain, stooling frequency, incidence of constipation, diarrhea and regurgitation between two groups ($p>0.05$). No adverse effects related to will fumitory and simethicone group were observed. **Conclusion:** Will fumitory make a considerable improvement in colic related crying in comparison with simethicone. It was also well tolerable by infants suggesting as a new therapeutic approach in infantile colic.

**Keywords:** *Fumaria parviflora* Lam., Infantile Colic, Simethicone, Will fumitory.

**Correspondence:**
**Dr. Ali Mohammad Ranjbar**
[1]Department of Pharmacognosy, Faculty of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, IRAN.
[2]Department of Pharmacognosy, Traditional Pharmacy and Pharmaceutical Sciences Research Center, Faculty of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, IRAN.
Email: amranjbar@alumnus.tums.ac.ir

**Received:** 13-08-2024;
**Revised:** 22-01-2025;
**Accepted:** 07-05-2025.

## INTRODUCTION

Infantile colic is one of the most common issues of infancy.[1] Approximately 1 in 5 infants experiences colic during first few months of life.[2] Clinical diagnosis of colic is most commonly based on the modified Wessel's criteria: crying for no identifiable reason lasting ≥3 hr per day for ≥3[3] days per week in a healthy infant.[4] Although the pathophysiological mechanisms of infantile colic are still unknown briefly, but excessive intestinal gas production, gut inflammation, immaturity of enteric nervous system and lactase deficiency have been hypothesized confirming the role of gastrointestinal issues in the etiology of colic,[3,5] while some investigations demonstrate intestinal hypermotility due to increased motilin and ghrelin levels in colicky infants resulting in increased gastric emptying and intestinal peristalsis.[6] Associations between postpartum depressive disorder, earlier breastfeeding cessation and colic have been reported.[7]

Recommended treatments for infantile colic include behavioral, nutritional and pharmacological interventions, although there is not enough evidence to support the efficacy of behavioral interventions.[8] Hydrolysate formulas for bottle-fed infants or hypoallergic diets in breastfeeding mothers could be helpful in some cases of infantile colic.[9] Dicyclomine hydrochloride is effective as an anticholinergic drug which leads to smooth muscle relaxation and consequent antispasmodic effect. It should be noted dicyclomine is contraindicated due to serious side effects in infants.[8] The efficacy of herbal antispasmodic agents was investigated in traditional medicine[10] as well as conventional phytotherapy.[11]

*Fumaria parviflora* Lam. (*Fumariaceae*), known as will fumitory, is a small, creeper, branched, annual herb growing wild in Asia, Europe and Africa.[12] Phytochemical profile of will fumitory includes organic acids and isoquinoline alkaloids such as fumaric acid, caffeic acid, aldumiceine, coptisine, protropine,

**DOI:** 10.5530/pres.20251909

sinactine, cryptopine, fumariline, fumaritine, fumarophycine, O-Methylfumarophycine, palmatine, parfumine, stylopine and N-methyl stylopine.[13]

Will fumitory is applied in the treatment of dermatological disorders, hepatobiliary dysfunctions, gastrointestinal issues such as dyspepsia, constipation and abdominal cramp in Iranian medicine[14] as well as anti-scorbite, anti-scabies, anti-bronchitis, anti-pyretic, diuretic, diaphoretic, expectorant, appetizer and antineoplastic potencies.[15] Through recent studies, will fumitory has antinociceptive,[16] hepatoprotective,[17] nematocidal[18] acetylcholinesterase and botyrylcholinesterase inhibitory effects.[19] Furthermore, both smooth muscle relaxant activity and spasmogenic effects of will fumitory have been demonstrated by *in vitro* studies.[20]

The present study was conducted to evaluate the effect of the aqueous extract of will fumitory on infantile colic referred to the Khatam-Al-Anbia multi-specialty clinic in Yazd, Iran.

## MATERIALS AND METHODS

### Plant material

Flowering aerial parts of will fumitory was collected in March-April 2017 from Yazd province, Iran. The botanical authentication was made by the department of Pharmacognosy, Faculty of Pharmacy, Shahid Sadoughi University of Medical Sciences and Health Services, Yazd, Iran.

### Preparation of extract

The plant material was cleaned and dried in shade and then it was cut into pieces about 1-2 cm. Out of 200 g of plant sample was extracted by 2000 mL distilled water in a reflux system at 80°C for 90 min. The extract was filtered through Whatman no.1 filter paper (GE Healthcare, UK) and stored at 4°C in dark bottles.

### HPLC analysis

Determination of fumaric acid content was performed by a HPLC method set by Shui *et al.*[21] All reagents were HPLC grade. Methanol and sulfuric acid were purchased from Merck (Germany) and fumaric acid was purchased from Sigma-Aldrich (Germany).

A D-14163 smart line HPLC Series system (Knauer, Germany) was employed consisting of a smart line manager, a degasser (smart line 5000), a pump (smart line 1000) and a fluorescent Detector (RF 10AXL, Shimadzu, Japan). The stationary phase was Perfectsil target (MZ-Analysentechnik, Germany) ODS-3 C18 column (250×4.6 mM i.d., 5 µM particle), which was maintained at 40°C. The mobile phase consisted of sulfuric acid in double distilled water (pH=2.5) and methanol. The flow-rate of sulfuric acid was 0.35 mL.min$^{1}$ and the flow-rate of methanol was from 0 to 0.45 mL.min$^{-1}$ from 15 to 75 min. The injection volume was 20 µL and the UV detection was performed at 215 nm. The calibration curve was constructed based on fumaric acid concentrations of 2, 5, 10, 15 and 20 µg.mL$^{-1}$ in sulfuric acid (pH=2.5).

### Subjects

The present study followed a randomized double-blind clinical trial conducted during May to December 2017; Out of 49 exclusively breast-fed colicky infants referred to the pediatrics department of Khatam Al-Anbia Multi-Specialty were involved in the study. They were 3 to 8 weeks, with appropriate gestational age and birth weights between 2500 and 4000 g, diagnosed with infantile colic based on modified Wessel's criteria, defined as cry-fuss behavior lasted ≥3 hr a day for ≥3 days in one week, before enrollment. The whole infant underwent a clinical evaluation conducted by pediatrician. Exclusion criteria were set as clinical evidence of gastrointestinal disorders or chronic illnesses. The mothers were asked to avoid cow's milk in their diet.

### Study Design

The enrolled Infants were randomly assigned to receive either will fumitory extract or simethicone (DicolicGut, Iran) which were supplied in a 30 mL dark bottle with a dropper cap, three times a day for 10 days before feeding and parents were asked to refrigerate it.

Demographic information including types of delivery, gender, birth weight, entry weight, entry age, birth order, family history of atopy and history of exposure to smoking were obtained. The Parents were asked to fill a daily note about infant crying duration, stooling frequency and consistency during the study. Weight gain as a growth parameter was measured during the study. Intervention tolerability and side effects including diarrhea, constipation, vomiting and cutaneous reactions were assessed according to Savino's study.[22]

### Statistical Analysis

Clinically relevant difference was set where crying duration was reduced more than 50 min according to Savino's study.[23] Considering α=0.05, β=0.20 and possible follow up loss of 20%, the sample size was calculated to be 26 in each group. Data have been presented as mean±standard deviation and compared using unpaired Student's *t*-test, Mann-whitney test and Fisher's exact test as appropriate. Responder information was evaluated on an intention-to-treat basis, wherein the infants who dropped out from will fumitory extract group were regarded as non-responders and those who dropped out from simethicone group were mentioned as responders. *p* value <0.05 was statistically significant and SPSS 16 (SPSS Inc, Chicago, IL) was applied in data analysis.

### Study Objectives and Outcomes

Primary outcome was defined as reduction in average crying duration to less than 180 min per day according to Wessel's

criteria.[4] Secondary outcome was set as the number of responders in each group at the end of study who demonstrated ≥50% reduction in average crying duration.

## RESULTS

### Fumaric acid content

Based on Shui *et al.*,[21] study, the content of Fumaric acid was 11.0±2.3 μg.mL$^{-1}$ where retention time and LOD were 24.6 min and 0.17 μg.mL$^{-1}$, respectively. The HPLC chromatogram of will fumitory aqueous extract is presented in Figure 1.

### Demographic and clinical characteristics

Among 95 infants diagnosed with infantile colic, 43 subjects were excluded based on exclusion criteria ($n$=18) or the parents did not give informed consent ($n$=25). The remaining 52 infants were divided randomly into 2 groups by random number method. Three patients (one in will fumitory group and two in simethicone group) discontinued intervention for no apparent reason. A total of 49 infants completed the study: 25 in the will fumitory group and 24 in the simethicone group (Figure 2).

There were no statistical differences between the groups about delivery type, gender, birth weight, entry weight, entry age, birth number, family history of atopy and exposure to smoking ($p$ value >0.05) (Table 1).

### Clinical outcomes

At enrollment, no significant difference was observed in daily median crying duration (min.day$^{1}$) between groups ($p$=0.714) while at the end of the study, infants receiving will fumitory extract demonstrated a significant reduction in crying duration in comparison with simethicone group ($p$<0.001) (Table 2). Based on secondary outcome criteria, duration of crying in 25 patients in will fumitory group were reduced, whereas in simethicone group response was.

### Tolerance

Average weight gain during the study period was comparable between the will fumitory group and simethicone group ($p$ value>0.05). There were no significant differences in the case of stooling frequency and consistency between the groups. Reported adverse events during the study were eczema in will fumitory group ($n$=1) and gastroesophageal reflux in simethicone group ($n$=1) and will fumitory group ($n$=1) which were unrelated to intervention.

## DISCUSSION

Infantile colic is recognized as excessive and inconsolable crying in otherwise healthy and well-fed babies without unexplained character, which usually emerges in the first few weeks of life and diminishes by age 4 to 5 months. Despite consideration as self-limiting condition, infantile colic by occurring 1 in 6 families caused to the main hardship for the infant, family and health care givers.[5,24]

In this study we investigated the efficacy and tolerability of will fumitory extract in infantile colic against simethicone, as one of the standard treatments for infantile colic.[25]

Infants receiving will fumitory extract demonstrated significant reduction in daily crying duration (primary outcome) and analysis of responders revealed that whole infants experienced ≥50% reduction in crying duration which is clinically considerable.[26]

Oral administration of will fumitory extract was reported to decrease frequency and length of crying periods besides number of times an infant wake up due to colic pain in a primary study conducted by Montasery *et al.*,[27] although dose of administration based on fumaric acid, method of extraction and the species of will fumitory were not specified in the study.

The gastric pain relief effect of will fumitory was also observed in another clinical study in which administration of 1,500 mg fumitory extract, 3 times daily reduced the pain in IBS patients.[28]

Will fumitory supposed to have spasmolytic and smooth muscle relaxant activities and as a result has been traditionally used in gut disorders includes diarrhea, abdominal cramps and indigestion.[14,29] An *in vivo* study illustrated *Fumaria capreolata* possesses anti-inflammatory effect through inhibition the secretion and expression of Interleukin-6 (IL-6) and Tumor Necrosing Factor- α (TNF-α) in colon tissue as well as inhibition transcription of pro-inflammatory mediators.[30] This anti-inflammatory effect can probably explain the role of will fumitory in infantile colic amelioration.

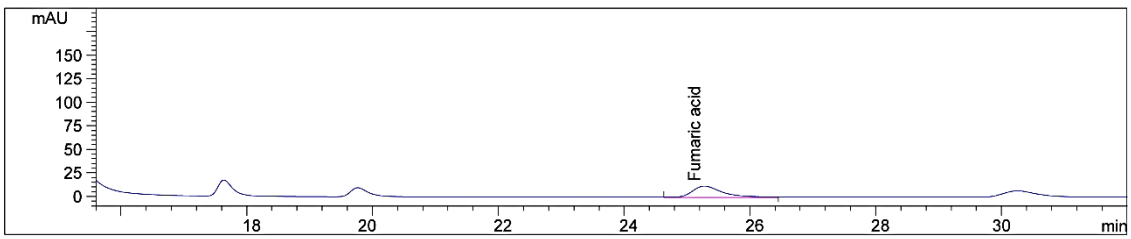


**Figure 1:** The HPLC chromatogram of will fumitory aqueous extract.

**Table 1: Baseline characteristics of participants in the study groups.**

| Variable[a] | will fumitory (*n*=25) | Simethicone(*n*=24) | *p*-Value |
|---|---|---|---|
| Delivery, spontaneous/caesarean (n) | 8/17 | 10/14 | 483[b] |
| Gender, male/female (n) | 12/13 | 11/13 | 879[b] |
| Age at entry (day) | 35.8±11.8 | 38.7±11.9 | 395[c] |
| Birth weight (g) | 3121.6±466.4 | 3233.3±352.2 | 350[c] |
| Entry Weight (g) | 4353.2±763.9 | 4400±609.7 | 814[c] |
| First child, yes/no (n) | 8/17 | 7/17 | 830[b] |
| family history of atopy, yes/no (n) | 3/22 | 3/21 | NS[b] |
| History of exposure to smoking, yes/no (n) | 2/23 | 2/23 | NS[b] |

NS indicates not significant.[a] data are presented as Mean±Standard deviation or number.[b] Fisher's exact test.[c] Student's *t* test.

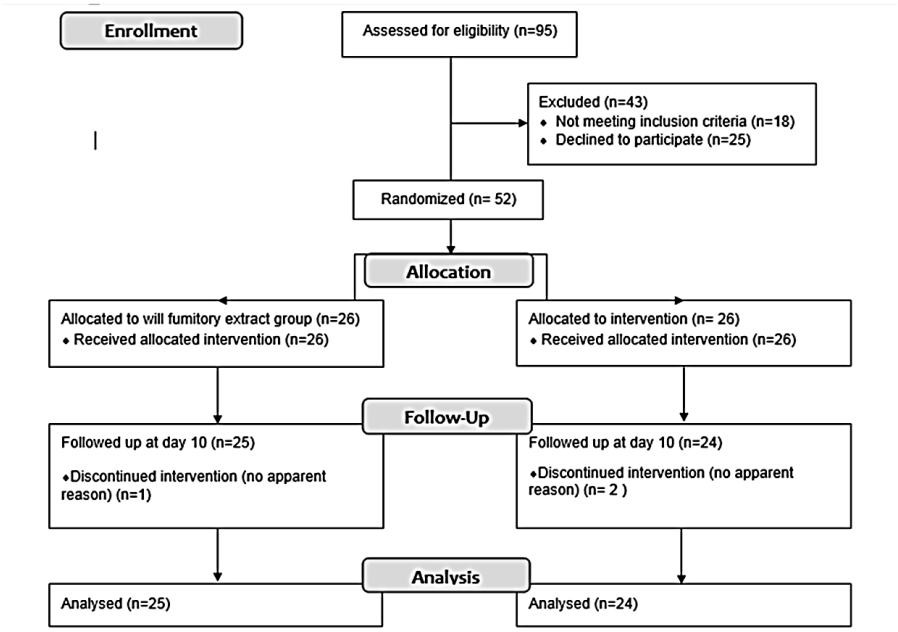


**Figure 2:** Diagram of patient enrollment and study process.

The mentioned probable mechanism is in accordance with study conducted by Vezza *et al.*, where concluded total alkaloid fraction of *Fumaria capreolata* L. extract exerts reduction in macroscopic and microscopic signs of intestinal inflammation through affecting colonic expression of pro-inflammatory and anti-inflammatory mediators besides barrier markers.[31]

Likewise, Bashir *et al.*, showed that will fumitory aqueous-methanolic extract could improve castor oil induced diarrhea in mice and rats similar to both dicyclomine and loperamide which can be explained by tonic inhibition of rat colon contractile activity through dual blockage of muscarinic receptors and $Ca^{2+}$ channels.[20]

It should be noted that based on an *in vitro* study by Gilani *et al.*, a dose-dependent spasmogenic effect declining at higher doses was observed from aqueous-ethanolic extract of will fumitory. The maximum spasmogenic effect perceived was 45.5±1.06% of the acetyl choline (10 µM) maximum. It might be due to either the partial agonist activity of the extract or some spasmolytic factors don't let spasmogenic effect going beyond a certain limit.[32] It was also claimed that the stimulatory constituents become more active in constipated gut, while spasmolytic effects become more evident in hyperactive intestinal situations[33] explaining the controversial effects of will fumitory on constipation and diarrhea.

Shakya *et al.*, showed that oral intake of *Fumaria indica* aqueous-ethanolic extract and fumaric acid as the plant active constituent could result in pain relieving effects comparable with pentazocine, a centrally active analgesic drug, in mice. Furthermore, both caused inhibitory effects against induced peripheral inflammation.[34]

Fumaric acid as an organic acid which was identified in our extract 11.0±2.3 µg.mL$^{1}$, is considered as effective component of the genus Fumaria to anti-inflammatory, immunomodulatory

**Table 2: Parameters associated with tolerability in study groups.**

| Variable | will fumitory (*n*=25) | Simethicone (*n*=24) | *p*-Value |
|---|---|---|---|
| Weight gain during study, mean±SD (g). | 273.2±73.18 | 273.3±79.33 | 995[a] |
| Stooling frequency at entry, median (IQR) (n/day). | 3(4.5) | 3(4.75) | 436[b] |
| Stooling frequency at 10$^{th}$ day, median (IQR) (n/day). | 3(4.5) | 4(5.5) | 456[b] |
| Constipation reported among infants (n). | 0 | 2 | 235[c] |
| Diarrhea reported among infants (n). | 2 | 2 | NS[c] |
| Regurgitation reported among infants (n). | 2 | 0 | 49[c] |

There were no significant differences between the groups. NS indicates not significant. [a]Student's *t* test. [b]Mann-Whitney test. [c]Fisher's exact test.

and antioxidant activities.[30] Active metabolites of fumaric acid esters (monomethyl fumarate and dimethyl fumarate) have been demonstrated to possess immunomodulatory effects on psoriasis through stimulating TNF-α and producing antagonists of IL-10 and IL-1 receptors in human peripheral blood mononuclear cells[35] which could be in accordance to the present study.

## CONCLUSION

Our findings revealed that will fumitory aqueous extract could be a new therapeutic approach to infantile colic based on therapeutic considerable effect and proper tolerance criteria. Additional research is needed to define the best dose of extract as well as dosage form development to improve formulation factors. Furthermore, it is suggested to repeat the present study in larger sample sizes and longer durations.

## ACKNOWLEDGEMENT

The authors would like to express their appreciation to Shahid Sadoughi University of Medical Sciences and whole individuals whose contributed and supported present study, emotionally and intellectually, in special Dr. Mohammad Reza Shams Ardekani for his kindly guidance.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest. The authors alone are responsible for the accuracy and integrity of the paper content.

## FUNDING

This work was supported by a grant (No: 4556) from Shahid Sadoughi University of medical Science, Yazd, Iran.

## ABBREVIATIONS

**HPLC:** High performance liquid chromatography; **TNF-α:** Tumor necrosing factor- α; **IL:** Interleukin.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Study protocol was confirmed by the ethics committee of Shahid Sadoughi University of Medical Sciences (ethics code: Ir.ssu.medicine.rec.1395.212). The study was registered at the Iranian Clinical Trial Registration Center with the number IRCT20140817018828N5 and written informed consent was acquired from parents before enrollment.

## SUMMARY

Infantile colic is a prevalent issue in approximately 20% of infants, which is diagnosed based on the Wessel's criteria. Some therapeutic interventions are suggested to modify infantile colic, but lack of efficacy and serious side effects limit their administration. Conventional phytotherapy as well as traditional medicine demonstrated efficacy of herbal antispasmodic agents. *Fumaria parviflora* Lam., known as will fumitory, is used to treat gastrointestinal disorders including constipation, dyspepsia and abdominal cramp in Iranian medicine; on the other hand, experimental studies illustrated their smooth muscle relaxant activity and spasmogenic effects. The present study aimed at evaluation effect of the aqueous extract of will fumitory on infantile colic referred to the Khatam-Al-Anbia multi-specialty clinic in Yazd, Iran. After preparation aqueous extract, its fumaric acid content was determined by HPLC analysis. Through a double-blind clinical study on 52 infants, efficacy of will fumitory extract and simethicone in changing in infants' colic symptoms including stooling frequency, duration of crying and consistency as well as probable side effects for 10 days were evaluated. Will fumitory lead to a considerable improvement in colic related crying in comparison with simethicone. It was also well tolerable by infants suggesting as a new therapeutic approach in infantile colic.

## REFERENCES

1. Turner TL, Palamountain S. Infantile colic: clinical features and diagnosis. UpToDate. 2015.
2. Wake M, Morton-Allen E, Poulakis Z, Hiscock H, Gallagher S, Oberklaid F. Prevalence, stability and outcomes of cry-fuss and sleep problems in the first 2 years of life: prospective community-based study. Pediatrics. 2006;117(3):836-42. doi: 10.1542/peds.2005-0775, PMID 16510665.

3. Sarasu JM, Narang M, Shah D. Infantile colic: an update. Indian Pediatr. 2018;55(11):979-87. doi: 10.1007/s13312-018-1423-0, PMID 29941700.
4. Wessel MA, Cobb JC, Jackson EB, Harris Jr GS, Detwiler AC. Paroxysmal fussing in infancy, sometimes called colic. Pediatrics. 1954;14(5):421-35. doi: 10.1542/peds.14.5.421, PMID 13214956.
5. Zeevenhooven J, Browne PD, l'Hoir MP, de Weerth C, Benninga MA. Infant colic: mechanisms and management. Nat Rev Gastroenterol Hepatol. 2018;15(8):479-96. doi: 10.1038/s41575-018-0008-7, PMID 29760502.
6. Savino F, Grassino EC, Guidi C, Oggero R, Silvestro L, Miniero R. Ghrelin and motilin concentration in colicky infants. Acta Paediatr. 2006;95(6):738-41. doi: 10.1080/08035250500522654, PMID 16754557.
7. Radesky JS, Zuckerman B, Silverstein M, Rivara FP, Barr M, Taylor JA, *et al.* Inconsolable infant crying and maternal postpartum depressive symptoms. Pediatrics. 2013;131(6):e1857-64-e64. doi: 10.1542/peds.2012-3316, PMID 23650295.
8. Johnson JD, Cocker K, Chang E. Infantile colic: recognition and treatment. Am Fam Physician. 2015;92(7):577-82. PMID 26447441.
9. Iacovou M, Ralston RA, Muir J, Walker KZ, Truby H. Dietary management of infantile colic: a systematic review. Matern Child Health J. 2012;16(6):1319-31. doi: 10.1007/s10995-011-0842-5, PMID 21710185.
10. Ardakani MR, Farjadmand F, Rahimi R. Makhzan al adviyeh and pointing to the scientific names of medicinal plants for the first time in a Persian book. Trad Integr Med. 2018:186-95.
11. Javan R, Feyzabadi Z, KIANI MA. Management of infantile colic; based on traditional Iranian medicine; 2015.
12. Mabberley DJ. The plant-book: a portable dictionary of the vascular plants. Cambridge university press; 1997.
13. Soušek J, Guédon D, Adam T, Bochořáková H, Táborská E, Válka I, *et al.* Alkaloids and organic acids content of eight Fumaria species. Phytochem Anal. 1999;10(1):6-11. doi: 10.1002/(SICI)1099-1565(199901/02)10: 1<6::AID-PCA431>3.0.CO;2-0.
14. Baquar SR. Medicinal and poisonous plants of Pakistan; 1989.
15. Zargari A. Medicinal plants. Tehran University of Medical Sciences; 1997.
16. MANDEGARI A, ENAYATI M. Antinociceptive effects and toxicity of *Fumaria parviflora* Lam. in mice and rats. 2004.
17. Tripathi M, Singh BK, Mishra C, Raisuddin S, Kakkar P. Involvement of mitochondria mediated pathways in hepatoprotection conferred by *Fumaria parviflora* Lam. extract against nimesulide induced apoptosis *in vitro*. Toxicol *Vitro*. 2010;24(2):495-508. doi: 10.1016/j.tiv.2009.09.011.
18. Naz I, Palomares-Rius JE, Saifullah BV, Blok V, Khan MR, Ali S, et al. *In vitro* and in planta nematicidal activity of *Fumaria parviflora* (Fumariaceae) against the southern root-knot nematode meloidogyne incognita. Plant Pathol. 2013;62(4):943-52. doi: 10.1111/j.1365-3059.2012.02682.x.
19. Orhan I, Şener B, Choudhary MI, Khalid A. Acetylcholinesterase and butyrylcholinesterase inhibitory activity of some Turkish medicinal plants. J Ethnopharmacol. 2004;91(1):57-60. doi: 10.1016/j.jep.2003.11.016, PMID 15036468.
20. Najeeb-ur-Rehman S, Bashir S, Al-Rehaily AJ, Gilani AH. Mechanisms underlying the antidiarrheal, antispasmodic and bronchodilator activities of *Fumaria parviflora* and involvement of tissue and species specificity. J Ethnopharmacol. 2012;144(1):128-37. doi: 10.1016/j.jep.2012.08.039, PMID 22975416.
21. Shui G, Leong LP. Separation and determination of organic acids and phenolic compounds in fruit juices and drinks by high-performance liquid chromatography. J Chromatogr A. 2002;977(1):89-96. doi: 10.1016/s0021-9673(02)01345-6, PMID 12456098.
22. Savino F, Cordisco L, Tarasco V, Palumeri E, Calabrese R, Oggero R, et al. *Lactobacillus reuteri* DSM 17938 in infantile colic: a randomized, double-blind, placebo-controlled trial. Pediatrics. 2010;126(3):e526-33. doi: 10.1542/peds.2010-0433, PMID 20713478.
23. Savino F, Pelle E, Palumeri E, Oggero R, Miniero R. *Lactobacillus reuteri* (American Type Culture Collection Strain 55730) versus simethicone in the treatment of infantile colic: a prospective randomized study. Pediatrics. 2007;119(1):e124-30. doi: 10.1542/peds.2006-1222, PMID 17200238.
24. Lucassen P. Colic in infants. BMJ Clin Evid. 2010; 2010.
25. Metcalf TJ, Irons TG, Sher LD, Young PC. Simethicone in the treatment of infant colic: a randomized, placebo-controlled, multicenter trial. Pediatrics. 1994;94(1):29-34. doi: 10.1542/peds.94.1.29, PMID 8008533.
26. Baldassarre ME, Di Mauro A, Tafuri S, Rizzo V, Gallone MS, Mastromarino P, *et al.* Effectiveness and safety of a probiotic-mixture for the treatment of infantile colic: a double-blind, randomized, placebo-controlled clinical trial with fecal real-time PCR and NMR-based metabolomics analysis. Nutrients. 2018;10(2):195. doi: 10.3390/nu10020195, PMID 29439395.
27. Montaseri S, Pourarian S, Montaseri H. Effects of Fumaria extract on colic pain in 3-16 weeks infants. Iran J Neonatol. 2013;4(2):10-5.
28. Brinkhaus B, Hentschel C, Von Keudell CV, Schindler G, Lindner M, Stützer H, *et al.* Herbal medicine with curcuma and fumitory in the treatment of irritable bowel syndrome: a randomized, placebo-controlled, double-blind clinical trial. Scand J Gastroenterol. 2005;40(8):936-43. doi: 10.1080/00365520510023134, PMID 16173134.
29. Mossa JS, Al-Yahya MA, Al-Meshal IA. Medicinal plants of Saudi Arabia; 1987.
30. Kiumarsi F, Derakhshan AR. Gastrointestinal and hepatic effects of Fumaria species in traditional Persian medicine and modern medical studies: A narrative review. J Sabzevar Univ Med Sci. 2022;29(5):697-718.
31. Bribi N, Rodríguez-Nogales A, Vezza T, Algieri F, Rodriguez-Cabezas ME, Garrido-Mesa J, *et al.* Intestinal anti-inflammatory activity of the total alkaloid fraction from *Fumaria capreolata* in the DSS model of colitis in mice. Bioorg Med Chem Lett. 2020;30(18):127414. doi: 10.1016/j.bmcl.2020.127414, PMID 32717615.
32. Gilani AH, Bashir S, Janbaz KH, Khan A. Pharmacological basis for the use of Fumaria indica in constipation and diarrhea. J Ethnopharmacol. 2005;96(3):585-9. doi: 10.1016/j.jep.2004.10.010, PMID 15619582.
33. Gilani AH, Rahman AU. Trends in ethnopharmacology. J Ethnopharmacol. 2005;100(1-2):43-9. doi: 10.1016/j.jep.2005.06.001, PMID 16127805.
34. Shakya A, Singh GK, Chatterjee SS, Kumar V. Role of fumaric acid in anti-inflammatory and analgesic activities of a Fumaria indica extracts. J Intercult Ethnopharmacol. 2014;3(4):173-8. doi: 10.5455/jice.20140912021115, PMID 26401369.
35. Asadullah K, Sterry W, Stephanek K, Jasulaitis D, Leupold M, Audring H, *et al.* IL-10 is a key cytokine in psoriasis. Proof of principle by IL-10 therapy: a new therapeutic approach. J Clin Invest. 1998;101(4):783-94. doi: 10.1172/JCI1476, PMID 9466973.


**Cite this article:** Ramezani V, NooriShadkam M, Ghiasirad M, Ebrahimi S, Ranjbar AM. *Fumaria parviflora* Lam. Aqueous Extract Versus Simethicone in the Treatment of Infantile Colic: A Prospective Randomized Clinical Trial. Pharmacog Res. 2025;17(3):867-72.