

Review Article

## *Prunus domestica* as effective and acceptable treatment for stool softening and relief of constipation symptoms

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### Abstract

Constipation, a worldwide gastrointestinal disorder needs to osmotic and stimulant laxatives. The use of herbal medicines as laxative agents is prevalent in folk and traditional medicines. *Prunus* L. and especially *P. domestica* delicious fruits are popular as remedy for constipation. According to traditional beliefs *P. domestica* relaxes the stomach and expels the yellow bile. According to traditional belief, we searched in different resources, books, thesis, etc. The results exhibited that *P. domestica* is used as mild to moderate laxative in modern medicines. The use of *P. domestica* is associated with normal bowel or gastrointestinal or colonic functions that are the result of reduction in transit time, bulking the stool, and increased in the frequency of bowel movement. *P. domestica* can be used in pregnant and breast-feeding mothers. The only adverse effect of *P. domestica* is its bloating effects in some clinical studies. *P. domestica* fruits can be used in laxative formulations with other laxatives or alone for improvement of gastrointestinal functions.

**Keywords:** *Prunus domestica*, prune, plum, constipation, bloating

### 1. Introduction

Constipation as a prevalent gastrointestinal disorder is associated with infrequent stool, painful and difficult evacuation. The average prevalence of constipation among the adult population is about 16% worldwide. Age, gender, diets with low fiber, diseases, medications, stress, travel, obesity, lack of exercise, family history of constipation are the etiology of constipation. The use of osmotic and stimulant laxatives is the first treatment strategies for management of constipation (Forootan, Bagheri, & Darvishi, 2018). Herbal medicines with laxative effects are used in different societies to overcome constipation (Iizuka & Hamamoto, 2015).

*Prunus* L. or “plum tree” in the Rosaceae family is popular due to its therapeutic effects (Mozaffarian, 1996). Three most important species of this genus including *Prunus domestica*, *Prunus salicina* and *Prunus americana* are consumed as food and medicine (Jabeen & Aslam, 2011). *P. domestica* delicious fruits have different size and color, which

are consumed mainly fresh and dried (Vakili, Ahmadi-pour, & Rahmani, 2018). *P. domestica* and *P. americana* are the most important medicinal plant for treatment of constipation in Iranian traditional medicine (Vakili *et al.*, 2018). According to the Iranian Traditional Medicine, *P. domestica* with traditional name of “Ojas” is known as the best laxative (Mozaffarpur *et al.*, 2012) and is used orally for treatment of constipation (Nimrouzi *et al.*, 2014). Traditional philosophers believed that prune relaxes the stomach and expels the yellow bile (Bae, 2014). *P. domestica* are used in India in treatment of leucorrhoea, and irregular menstruation (Kayano, Kikuzaki, Fukutsuka, Mitani, & Nakatani, 2002). In Iranian traditional medicine, *P. domestica* is used in the form of syrup for treatment of hot diseases such as hot headache and stomach disorders, due to cold and wet temperaments. For preparation of this syrup, *P. domestica* fruits and water are boiled and the filtrate is concentrated to the viscosity of 6.5. The viscous fruit concentrate is sweetened by adding sugar (1:2) and is heated until the sugar completely is dissolved. This syrup is suitable purgative agent without any adverse effects (Hamzeloo-Moghadam, Danaifar, Mostafavi, & Hajimehdipour, 2015). There are some review articles on pharmacological effects (Jabeen & Aslam, 2011) and health effects (Igwe & Charlton,

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2016) of *P. domestica*, but there is no review articles on its efficacy in management of constipation.

## 2. Chemical Composition of *Prunus domestica*

There are many biological compounds in *P. domestica* which are responsible for its biological activities. 3-O-caffeoylquinic acid, chlorogenic acid, 4-O-caffeoylquinic acid, 4-amino-4-carboxychroman-2-one, caffeoylquinic acid isomers are known in *P. domestica* and are responsible for its antioxidant activities (Kayano *et al.*, 2002). Organic acids (malic and citric, neochlorogenic, chlorogenic, caffeic acids), rutin, hydroxycinnamic acids, flavonoids, and anthocyanidins were identified in *P. domestica* (L. V. Lenchyk, 2016). Quercetin-3-O-glycoside, Kaempferol-3-O-glycoside, isoramnetin-3-o-glycoside, quercetin, kaempferol, isoramnetin, monosaccharids (glucose, rhamnose, galactose) are isolated from *P. domestica* leaves. Sucrose, glucose, fructose and sorbitol are the main carbohydrates (L. Lenchyk, 2016). The presence of anthocyanins in *P. domestica* fruits as the subclass of flavonoid content is related to health benefits (Igwe & Charlton, 2016). Cyanidin-3-glucoside, cyanidin-3-rutinoside, low amounts of cyaniding-3-xyloside, peonidin-3-rutinoside, and peonidin-3-glucoside are the major anthocyanins of *P. domestica* (Roussos, Efstathios, Intidhar, Denaxa, & Tsafouros, 2016). *P. domestica* is a main source of vitamins (ascorbic acid, B<sub>1</sub>, B<sub>2</sub>, B<sub>3</sub>, B<sub>5</sub>, B<sub>6</sub>, A, E, K<sub>1</sub>, folate), carotenoids ( $\beta$ -carotene,  $\alpha$ -carotene,  $\beta$ -cryptoxanthin, lutein, zeaxanthin) (Igwe & Charlton, 2016). Ascorbic acid is the major vitamin in *P. domestica*. Potassium and phosphorus are the major minerals in plum fruits (Roussos *et al.*, 2016). Therefore, *P. domestica* has different biological components with potency as laxative agents.

## 3. The Efficacy of *P. domestica* on Constipation

Evaluation the efficacy and safety of *P. domestica* on constipation and bowel movement was the subject of ten clinical trials (Table 1).

In randomized double blind placebo controlled parallel study, the effects of processed food containing *P. domestica* extract (3 g) (standardized to 30 mg mumeferul and 1.12 citric acid) for 12 weeks on 74 healthy Japanese participants with systolic blood pressure between 130-160 mmHg in comparison with placebo exhibited that *P. domestica* extract consumption reduced the diastolic blood pressure in patients with grade I hypertension, two weeks after *P. domestica* extract intake. Fatigue and bowel movements increased after *P. domestica* consumption. No adverse effect or abnormal changes were observed after consumption of *P. domestica* (Nishimura, Kume, Kadowaki, Gato, & Nishihira, 2017). Daily consumption of 50, 100 g/day dried *P. domestica* on bowel function of 48 postmenopausal women consuming 500 mg calcium and 400 IU vitamin D<sub>3</sub>, compared with control group was the subject of clinical study. A seven point scale, including stool consistency, straining and pain during bowel movement, feeling of constipation after bowel movement and the amount of stool at baseline, 3 and 6 months after beginning of study was evaluated in three groups. Thirteen, 16 and 13 participants completed the study in control, 50 and 100 g/day dried *P. domestica*, respectively. There was no significant difference between two groups in

regard of demographic properties (age, height, weight, BMI, last menstrual period) and physical activity. The average estimated fecal bulk was not significantly different between three groups after 6 months, compared the control group. The overall feeling of constipation and pain significantly increased in control group, compared to intervention groups. The feeling of pain significantly decreased in 100 g dried *P. domestica* after three months compared with 50 g dried *P. domestica* group. Daily consumption of dried *P. domestica* in postmenopausal women was not associated with unfavorable changes in bowel habits and decreased the pain and general feeling of constipation, compared to control group (Shamloufard, Kern, & Hooshmand, 2017). *P. domestica* consumption snack (100 Kcal serving) for 2 weeks in comparison with low fat cookies on 26 women with BMI 24-35 in a crossover randomized clinical study increased the intakes of calcium, potassium, fiber, riboflavin, and niacin. *P. domestica* intended to decrease the total fat and cholesterol intakes with no effects on plasma triglycerides. The participants who received dried *P. domestica* had softer stool consistency, compared to low fat cookies control group (Howarth, Petrisko, Furchner-Evanson, Nemoosek, & Kern, 2010). In one randomized clinical study, the efficacy of flaxweed seeds (10-15 g) and *P. domestica* (40-50 g) (n=87) for three weeks was compared to control on Hajj pilgrims volunteers. The volunteers in the intervention group daily consumed the flaxweed seeds and *P. domestica* before the lunch and dinner for three weeks. The control group (n=67) consumed daily food without any intervention and constipation was defined according to Rome III criteria. The participant health status and visual analogue scales (VAS), gastrointestinal function (pain, bleeding in the time of defecation, fullness, nausea, incomplete defecation, distention, reflux) and constipation were evaluated before and after treatment. At the base line, there was no significant difference in regard of demographic characteristics. A significant improvement in bowel habits and daily fluid intake were observed in intervention group. *P. domestica* plus flaxweed seeds significantly prevented the constipation and improved the gastrointestinal functions in regard of frequency of bowel movement, defecation, fullness feeling, reflux, distention, nausea, pain, defecation, bleeding and health status in comparison with control group (Pasalar, Lankarani, Mehrabani, Tolide, & Naseri, 2013).

The effects of 50 g *P. domestica* for 3 weeks in comparison with control group were evaluated on 60 elderly women with constipation. Each participant soaked *P. domestica* in water and ate it in the morning before breakfast. The constipation severity was evaluated based on the Rom III diagnostic criteria. The efficacy of treatment was determined on the base of demographic questionnaire and constipation scales. At the base line, there was no significant difference between two groups in regards of demographic properties. The severity of constipation was improved in the patients who received the *P. domestica* daily (Mansouri, Shahraki-Vahed, Shadadi, Sanchooli, & Arbabisarjou, 2018). Dried *P. domestica* (100 g) for 4 weeks in forty-one men with mild hypercholesterolemia significantly increased the fecal dry weight and consistency, without any gastrointestinal disorders like diarrhea or loose stool (Tinker, Schneeman, Davis, Gallaher, & Waggoner, 1991). Daily consumption of 100 g *P. domestica* in comparison with 75 g dried apples for three

Table 1. The clinical studies for *P. domestica* on constipation

Intervention	Control	Duration	Participants	Results	Adverse effect	
<i>P. domestica</i> extract (3 g)	Placebo	12 weeks	74 healthy Japanese participants systolic blood pressure between 130-160 mmHg	Improve the fatigue and bowel movements	No adverse effect or abnormal changes	(Nishimura <i>et al.</i> , 2017)
50, 100 g/day dried <i>P. domestica</i>	Control	6 months	48 postmenopausal women	No significant effect on estimated fecal bulk Reduction in feeling of pain and general feeling of constipation	No unfavorable changes in bowel habits	(Shamloufar <i>et al.</i> , 2017)
100 Kcal serving of <i>P. domestica</i> snack	low fat cookies	2 weeks	26 women with body mass index between 24 and 35	The greater intake of calcium, potassium, fiber, riboflavin, and niacin. Decrease the total fat and cholesterol intakes softer stool consistency	-	(Howarth <i>et al.</i> , 2010)
flaxweed seeds (10-15 g) plus <i>P. domestica</i> (40-50 g)	Control	3 weeks	Hajj pilgrims volunteers	Improvement in bowel habits, and the amount of daily fluid intake prevent the constipation improvement the gastrointestinal functions	-	(Pasalar <i>et al.</i> , 2013)
50 g <i>P. domestica</i>	control	3 weeks	elder women	Improvement in constipation severity	-	(Mansouri <i>et al.</i> , 2018)
100 g <i>P. domestica</i>	75 g dried apples	3 months	38 postmenopausal women lacking of constipation	significant effect on fecal dried and wet weights, the fiber intake, and fecal bulk	No unfavorable effect in bowel habits.	(Lucas <i>et al.</i> , 2004)
100 g dried <i>P. domestica</i>	grape-juice-control period	4 weeks	Forty-one men with mild hypercholesterolemia	Increase in dry weight and fecal consistency	without any gastrointestinal disorders like diarrhea or loose stool	(Tinker <i>et al.</i> , 1991)
125 ml <i>P. domestica</i> juice	-	twice daily for 2 weeks	54 adults with gastrointestinal problem	positive effects on gastrointestinal functions Reduction in Difficult defecation.	Acceptable taste of <i>P. domestica</i> juice occurrence of flatulence and abdominal pain	(Pirainen <i>et al.</i> , 2007)
50 g/day dried <i>P. domestica</i> (n=20)	11 g psyllium (n=20)	three weeks with 1 week wash-out period	40 patients with chronic constipation	Increase in fecal bulk Improvement in complete bowel softer stool, higher stool consistency score, straining scores, overall constipation symptoms scores Better efficacy of <i>P. domestica</i> than psyllium	well tolerated No significant difference in postprandial fullness and bloating scores No adverse effects	(Attaluri <i>et al.</i> , 2011)
<i>P. domestica</i> juice	psyllium plus fiber free apple juice	prior to meal for 14 days	in 36 adults with chronic constipation	Increase the daily number of bowel movement, mean consistency rates, softer stool and constipation relief	-	(Cheskin <i>et al.</i> , 2009)

months was evaluated on bowel habits (frequency of defecation, fecal bulk and stool consistency) of 38 postmenopausal women lacking of constipation. On the base seven day validated bowel movement questionnaires, at the baseline and every month for the period of three months, the stool consistency (very soft to very hard), straining during bowel movement (none to extreme), pain during bowel movement (none to extreme), and constipation feeling after bowel movement was compared. There was no significant difference between two groups in regard to age, weight, BMI

at the baseline. *P. domestica* consumption increased the total energy, protein and carbohydrate uptakes, without significant effect on weight gain. *P. domestica* had no significant effects on bowel habits of postmenopausal women. Dried *P. domestica* had no unfavorable effect on bowel habits. *P. domestica* consumption had significant effect on fecal dried and wet weights, the fiber intake, and fecal bulk (Lucas, Mocanu, Smith, Soung, & Daggy, 2004). In other study, the laxative effects of 125 ml *P. domestica* juice, twice daily was evaluated on gastrointestinal functions of 54 adults (22-48

years old) for two weeks. The duration of study was four weeks including one week baseline period; two weeks period of *P. domestica* juice and one week follow up. The fecal frequency, difficult defecation, stool consistency, and gastrointestinal symptoms (diarrhea, flatulence, and abdominal pain) were assessed. The result of clinical study showed *P. domestica* juice decreased the occurrence of difficulty in defecation, and this effect continued to the follow up week. *P. domestica* juice increased the fecal bulk. The regular consumption of *P. domestica* juice had positive effects on gastrointestinal functions after two weeks. Difficulty in defecation decreased from 47% at baseline to 31% after two weeks of *P. domestica* juice consumption and 35% after one week follow up. Consumption of *P. domestica* juice was associated with occurrence of flatulence and abdominal pain ( $p=0.02$ ). The taste of *P. domestica* juice well accepted and tolerated (Piiirainen, Peuhkuri, Bäckström, Korpela, & Salminen, 2007). Dried *P. domestica* in comparison with psyllium was evaluated in patients with chronic constipation. In eight weeks single blind randomized cross over clinical study, two groups of patients received 50 g/day dried *P. domestica* fruits ( $n=20$ ) or 11 g psyllium ( $n=20$ ) for three weeks with 1 week wash-out period. The daily symptoms of patients and stool diary and consistency, the number of spontaneous bowel movement per week, global relief for constipation, straining, taste and tolerability were determined. A significant increase in number of complete spontaneous bowel movement per week was observed for dried *P. domestica* than that of psyllium treatment. Softer stool and higher stool consistency score were observed for dried *P. domestica* compare with psyllium. The means of straining scores was improved and were the same for psyllium and *P. domestica*, respectively. The overall constipation symptoms scores improved in two groups, but it was better in dried *P. domestica* group (1.7) than the psyllium group (1.3) ( $p=0.1$ ). *P. domestica* and psyllium are well tolerated with the same taste and satiety scores. The postprandial fullness and bloating scores had no significant difference between the two groups. There was no significant difference between two groups in regard of adverse effects. No gas or bloating symptom was observed in this study as adverse effects. The result of this study exhibited that *P. domestica* had better efficacy in relief of bowel symptoms of adult constipation than psyllium (Attaluri, Donahoe, Valestin, Brown, & Rao, 2011). In a controlled clinical study, the daily consumption of *P. domestica* juice prior to meal for 14 days was evaluated on 36 adults with chronic constipation (less than 1 per day) in comparison with psyllium plus fiber free apple juice or apple juice. The bowel movements per week were  $11.9\pm 15.0$ ,  $9.5\pm 5.9$ ,  $10.0\pm 9.7$  for apple juice, apple juice plus psyllium and *P. domestica* juice, respectively. The daily number of bowel movements was  $1.2\pm 0.8$ ,  $1.2\pm 0.7$  and  $1.3\pm 0.7$ , respectively. The mean consistency rates were  $0.85\pm 0.38$ ,  $0.88\pm 0.5$ ,  $0.74\pm 0.41$  for apple juice, psyllium plus apple juice and *P. domestica* juice, respectively. The participants who consumed the *P. domestica* juice had softer stool than that of other groups. *P. domestica* juice as psyllium provided constipation relief within 24 h of first use. The taste of *P. domestica* juice is superior to psyllium. *P. domestica* juice is known as an effective and acceptable treatment is result in softer stool and immediate relief of constipation symptoms (Cheskin *et al.*, 2009).

The results of clinical studies exhibited that *P. domestica* juice is a suitable candidate for constipation by softening the stool, bowel movement and consistency of stool. The use of *P. domestica* is associated with normal bowel or gastrointestinal or colonic functions that are the result of reduction in transit time, bulking the stool, increased in the frequency of bowel movement.

*P. domestica* extract or its dried fruits has mild laxative effects. The softer stool related to *P. domestica* consumption is related to sorbitol, dietary fiber and polyphenols. Sorbitol by its humectant effects (Piiirainen *et al.*, 2007) increases the stool's moisture content and softens the stools, which is associated with laxative activities (Lever, Cole, Scott, Emery, & Whelan, 2014). The laxative effects of various polysaccharide fractions from *P. domestica* (125 and 250 mg/kg orally was confirmed in mice with constipation. Polysaccharides soften the animal feces (Narimanovna, Makhmadalievich, Djalilovich, Erkinovna, & Takhirovich, 2016). Also, the fibers and water-soluble polysaccharides and fibers are responsible for laxative effects. *P. domestica* extract increases the rate of intestinal passage of stool in mice (Senyuk, Bashar, & Lenchyk, 2017). *P. domestica* 80 and 120 g/day for 4 weeks in 120 healthy adults compared to control group increased the stool weight to 22.2 and 32.8 g/day compared with control group ( $-0.8$  g/day). The stool frequency was increased in 80 g/day *P. domestica* (6.8) higher than that of 120 g/day (5.6). *P. domestica* had no effects on whole gut transit, which was associated with flatulence in healthy participants. The poorly fermented *P. domestica* fiber mechanically stimulates the gastrointestinal peristalsis, and increases the stool water and fiber. *P. domestica* significantly increased the bowel movements than the control group (Lever, Scott, Louis, Emery, & Whelan, 2019). *P. domestica* can be the source of some yeast isolates with ability of producing the organic acids such as acetic, citric, succinic and malic acids (Garcia-Fraile, Silva, Sanchez-Marquez, Velazquez, & Rivas, 2013). The prebiotic effects of prune fruit extract was confirmed against *Bifidobacterium bifidum* and *Lactobacillus rhamnosus* (Filimonova, Sahlanee, Senyuk, & Kononenko, 2019). Also, the sugar alcohols in *P. domestica* encourage the growth of acid producing intestinal microflora (Dikeman, 2004). *P. domestica* consumption increased the *Bifidobacteria* groups in human gut without any effects on short chain fatty acids and stool pH (Lever *et al.*, 2019).

#### 4. Safety of *P. domestica*

The recommended daily dose for *P. domestica* is 40-100 g, equivalent to three dried fruits. The acute oral toxicity of *P. domestica* crude extract is upper the dose of 5 g/kg. *P. domestica* Juice or its juice extract had no mutagenic effects in Ames test using *Salmonella typhimurium* TA98, TA100, TA1535, TA1538 with and without S9 (Luo *et al.*, 1991). 5 ml/kg *P. domestica* extract for 3 weeks had no effects on diuresis volume of diurnal diuresis of rats with erythrocyte hemolysis, but an increase in urine creatinine was observed, which implied on its ability to eliminate uric acid and creatinine from the body (L. V. Lenchyk, 2016). *P. domestica* can be used in pregnant woman and breastfeeding mothers with ferrous fumarate. A significant reduction in fecal pellet number, weight and percent moisture of stool was observed in the rats consuming the ferrous fumarate. *P. domestica* juice

significantly reduced the colon transit of feces and increased the fecal moisture and gastrointestinal movements. *P. domestica* juice regulated the intestinal movement and normalized the bowel movement in pregnant rats consuming  $\text{Fe}^{2+}$  (H, 2013). *P. domestica* consumption was associated with flatulence in healthy individuals (Lever *et al.*, 2019). Prosman (*P. domestica*) extract 100 mg for 12 weeks on 140 male (40-65 years old) had no effects on liver enzymes (serum aspartate transaminase (AST or SGOT) and alanine transaminase (ALT or SGPT), alkaline phosphatase (ALP) activities), urea and creatinine levels as hematological parameters (Sankhwar, Goel, & Tiwari, 2017). Therefore, *P. domestica* can be used as safe treatment for constipation.

## 5. Conclusions

Dried *P. domestica* is used for treatment of mild to moderate constipation (Scott & Knowles, 2011). Although the popular biological activity of *P. domestica* is its laxative effects, the other biological activities of *P. domestica* were the subject of research studies. *P. domestica* extract inhibited the entry of Hepatitis C virus into the cells and prevented infection (Bose *et al.*, 2017). Due to phytosterols, pentacyclic acid and ferulic acid esters contents of *P. domestica* extract, *P. domestica* showed the anti-inflammatory, and anti-edema effects in prostate diseases, which reduced the prolactin and accumulation of cholesterol in the prostate (Sankhwar *et al.*, 2017). *P. domestica* bark extract was a safe treatment to ameliorate the symptom of BPH in male Wistar rats (Swaroop, Bagchi, Kumar, Preuss, & Bagchi, 2015). The immunomodulatory effects of *P. domestica* were confirmed by augmentation of spleen cell proliferation in chickens with coccidiosis (Lee *et al.*, 2008). *P. domestica* consumption significantly reduced the blood pressure, cholesterol and LDL with an increase in HDL level (Ahmed, Sadia, Batool, Janjua, & Shuja, 2010). Pectin as soluble dietary fiber had lowering effects on blood cholesterol and LDL, while insoluble dietary fibers had bulking fecal effects (Garcia-Fraile *et al.*, 2013). Pectin due to viscous, gel forming properties had little effects on whole gastrointestinal transit time and delayed gastric emptying (Lever *et al.*, 2019). *P. domestica* snack before a meal decreased the energy intake, hunger, desire to eat and motivation to eat and increased the feeling of satiety in forty five healthy normal weight subjects without any effects on VAS ratings, feelings of thirst and pleasures compared to control group (Farajian, Katsagani, & Zampelas, 2010). The soluble and insoluble fiber contents of *P. domestica* are directly correlated with its laxative effects. The xylitol content of *P. domestica* reduces the intestinal transit time and increases the gastric emptying (E. K. Salminen *et al.*, 1989). Consumption of *P. domestica* has positive effects on intestinal microbiota and change them to acid producing one (S. Salminen, Salminen, Bridges, & Marks, 1986). *P. domestica* had no effects on adverse effects (heartburn, acid reflux, nausea, belching, borborygmi, abdominal bloating, abdominal pain/discomfort) and is used for treatment of mild to moderate constipation (Scott & Knowles, 2011). Carbohydrates (sucrose, glucose, fructose and sorbitol) (L. Lenchyk, 2016) along with dietary fibers and polyphenols in *P. domestica* decreased the occurrence of difficulty in defecation and transit time, increased the fecal bulk, the number of complete

spontaneous bowel movement, softening and bulking the stool (Narimanovna, Makhmadalievich, Djalilovich, Erkinovna, & Takhirovich, 2016). Sorbitol by its humectant effects (Piirainen *et al.*, 2007) increases stool moisture content and softens the stools (Lever, Cole, Scott, Emery, & Whelan, 2014). The poorly fermented *P. domestica* fibers mechanically stimulate the gastrointestinal peristalsis, and increase the stool water and fibers. Prune fruit extract has prebiotic effects against *Bifidobacterium bifidum* and *Lactobacillus rhamnosus* (Filimonova, Sahlanee, Senyuk, & Kononenko, 2019). The sugar alcohols in *P. domestica* encourage the growth of acid producing intestinal microflora (Dikeman, 2004).

Although there are several clinical trials on efficacy of *P. domestica* fruits on constipation in clinical studies, it is essential to design the clinical studies on its efficacy on constipation of pregnant women and breast feeding mothers.

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