Research Article

Antidiarrheal Effects of *Prosopis farcta* L. Fruit Extract: An Enteropooling and Histopathological Study in Rats

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Abstract | The aim of this study was to examine the antidiarrheal activity of the alcoholic fruit extract of *Prosopis farcta* L. in a rat model. Thirty male Albion Wistar rats randomized into six equal groups of five as follows: negative control (received distilled water), positive control (induced diarrhea with 2 ml castor oil), and experimental groups that received 2 ml castor oil followed by oral administration of different doses of *Prosopis farcta* L. fruit ethanolic extract (300 mg/kg, 400 mg/kg, and 500 mg/kg). A comparative group received castor oil along with loperamide (2.5 mg/kg) orally. The outcomes demonstrated that after three hours, the castor oil-treated animals produced liquid feces. Enteropooling test findings revealed that castor oil generated an accumulation of water and electrolytes in the intestinal loop. Weight and volume of the intestine were reduced after treatment with the fruit extract of *Prosopis farcta* L. In contrast to loperamide, all groups intestinal contents varied significantly (P≤0.05) in volume and weight. Histopathological examinations of the duodenum corroborated the antidiarrheal efficacy of the extract. In contrast to the positive control group, which showed significant edema and inflammatory cell infiltration, rats treated with the *Prosopis farcta* L. fruit extract exhibited varying degrees of tissue recovery. Particularly, the group receiving 500 mg/kg showed mild lesions and lower inflammatory cell infiltration, closely resembling the histological profile of the loperamide-treated group. Subsequent phytochemical analysis revealed the presence of tannins, carbohydrates, phenols, resins, flavonoids, saponins, alkaloids, coumarins, terpenes, and glycosides, while steroids and proteins were absent. The extract displayed antidiarrheal activity comparable to loperamide, showing a significant reduction in intestinal content volume and weight (P≤0.05). In conclusion, the ethanolic extract of *Prosopis farcta* L. fruits demonstrated promising antidiarrheal activity, potentially due to the phytochemical constituents identified, warranting further research for clinical applications.

Keywords | Antidiarrheal, Castor oil, Extract, *Prosopis Farcta,* Herbal Medicine, Rats.

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INTRODUCTION

One of the main causes of death and morbidity in underdeveloped nations is diarrhea which is an intestinal disturbance marked by the passing of three or looser and/or watery stools each day (Awe et al., 2011). Additionally, numerous studies on cattle and feedlot operations have demonstrated that animal pests directly affect economic factors like mortality, carcass features, and weight increase. Inflammation and diarrhea increase the risk of death and negatively affect the characteristics of animal carcasses, which results in large economic losses (Anaam et al., 2015; Mahmood et al., 2015; Medeiros et al., 2020). Gained growing attention as an opportunistic pathogen due to its links to additional intestinal infections, diarrhea with weakened immune systems (Hashim and Nema.,

2018). Dehydration, sadness, appetite loss, thick mucus, and severe diarrhea were among the animal's ailments (Hasso., 2018; Mikhael et al., 2023). When castor oil was used to produce diarrhea in rats, the extract had excellent antidiarrheal efficacy. Castor oil breaks down to recinolic acid in the small intestine, which is exceedingly irritating to the gut (Jaafar, 2010). Synthetic chemicals drugs such as loperamide used in the treatment of diarrheal diseases (Malinky et al., 2021). Loperamide, an opiate analogue, is a widely used anti-diarrheal agent and, until recently, its effects were attrilbuted to an inhibitory action on smooth muscle tone and peristalsis mediated via both cholinergic and non-cholinergic systems (Sandhu et al., 1981). Loperamide is inhibits local prostaglandin and acetylcholine release, decreasing peristalsis, by stimulating the gastrointestinal -opioid receptor. It has a good safety profile due to its low intrinsic bioavailability, high first-pass metabolism, and P-glycoprotein (P-gp) efflux, which reduces extra intestinal effects (Eggleston., 2016). Many plants species have long been found as an important source of drugs which have a therapeutic activity and for those medicinal plants are promising source of flavonoids, anti-inflammatory, antioxidant and antidiarrheal drug (Tungmunnithum et al., 2018; Hasan, 2019). One of the most well-known plants that have been employed in the treatment of illnesses is *Prosopis farcta* L. is a plant that it is an invasive weed that is very difficult to control. As supplementary food or drink for feeding buffalo, deer, antelopes, and other animals, they have also been used to make gum, paint, cordage, and other items. *Prosopis farcta* L. treat a variety of illnesses and conditions, including colds, measles, urinary tract infections, diarrhea, and diseases associated with swollen tissues (Asadollahi et al., 2014, Raoof and Dizaye, 2020). Fruits of *Prosopis farcta* L. have been used extensively in medicine as astringents, stomach tonics, blood coagulation agents, and anti-diarrheal (Safari et al., 2021). Studying to evaluate the antidiarrheal activity of *Prosopis farcta* L. fruits extract in rats comparing with Loperamide.

MATERIALS AND METHODS

Plant Materials and Extraction of *Prosopis farcta* L. Fruits

Ethical Approval

Ethical approval for this study was granted by the local committee of animal care and use at the College of Veterinary Medicine within the University of Baghdad (Approval Number: 11131 P.G, dated 22/5/2023).

Plant Materials Collection and Extraction

The *Prosopis farcta L.* fruits were bought from a local market in October 2022 from Baghdad city. The classification of the herb was done in the Ministry of Agriculture/ State Board for Seed Certification and Testing in Abu Ghraib, Baghdad) at the certification number 3366 in 14/11/2022. Fruit was washed, dried, and crushed. The crushed sample was weighed; Three hundred (300) g of powder of plant material *Prosopis farcta* L. fruits was put inside the flask and thousand (1000) ml of absolute ethanol 70% was added. The cold extraction by maceration method was for 24 hours. After that, the resulting cold extraction then was filtered through filter papers. Then, the extract was evaporated to dry by using a rotary evaporator. After that, the dry alcoholic extract was obtained and found to weighed. The final extract was kept in a sterile container in the freezer until use (Miri et al., 2020).

After two weeks of adaptation

Animals and Experimental Design

A total of 30 healthy young adults, male Wistar rats (*Rattus norvegicus*) weighing 200–250 g, and aged 8-10 weeks were obtained from the animal house at Baghdad University's Veterinary Medicine College Center. Animals were housed in plastic cages with 20×50×75 cm dimensions, placed in a special housing room belongs to the Department of Physiology, Biochemistry and Pharmacology, College of Veterinary Medicine, University of Baghdad . Before formally commencing the investigation, a four-weeks period for acclimatization was designated. Standard rodent diet (commercial feed pellets) and tap water were available ad libitum. Housing conditions were kept at 20-25 °C in air-conditioned rooms, and the light/dark cycle was 14/10 h. The air in the rooms was regularly replaced using ventilation vacuums.

Phytochemical Analysis

The phytochemical analysis of the ethanol extract was performed using standard qualitative methods (Harborne, 1998; Evans, 2009) to detect the presence or absence of various secondary metabolites, such as tannins, carbohydrates, glycosides, phenols, resins, flavonoids, saponins, alkaloids, proteins, coumarins, and terpenes and steroids.

Effect of *Prosopis farcta* L. Fruit Extract on Rat Enteropooling Induced by Castrol Oil

Six equal groups of thirty rats each will get castor oil treatment, with the exception of the negative control group.

Group 1: Negative control received just distilled water

Group 2: positive control received orally 2 ml of castor oil (Mascolo et al., 1993).

Group 3: received 300 mg/kg BW of *Prosopis farcta* L. fruit extract was administered orally after receiving 2 ml of castor oil (Mohammed and Kakey., 2020)

Group 4: 400 mg/kg B.W. of *Prosopis farcta* L. fruit extract was administered orally after receiving 2 ml of castor oil (Agirman et al., 2022).

Group 5: 500 mg/kg BW of *Prosopis farcta* L. fruit extract was administered orally after receiving 2 ml of castor oil

(Kadir et al., 2008).
Group 6: Administered oral Loperamide 2.5 mg/Kg BW after receiving castor oil 2 ml (Gilbert et al., 2014).

Table 1: Phytochemical tests for the ethanol extract of *Prosopis farcta* L. fruits

Phytochemical	Test Method	Reference
Tannins	Ferric chloride test	Jawad, 1997
Carbohydrates	Molisch's test	Du Mee & Vitex agnus castus, 1993
Glycosides	Keller-Killiani test	Jawad, 1997
Phenols	Ferric chloride test	Du Mee & Vitex agnus castus, 1993
Resins	Acetone test	Du Mee & Vitex agnus castus, 1993
Flavonoids	Shinoda test	Newall et al., 1996
Saponins	Froth test	McGuffin et al., 1997
Alkaloids	Dragendorff's test	Du Mee & Vitex agnus castus, 1993
Proteins	Biuret test	McGuffin et al., 1997
Coumarins	UV light test	Newall et al., 1996
Terpenes and steroids	Libermann-Burchard test	Jawad, 1997

Parameters

All the rats were sacrificed after two hours; the small intestine was then ligated and divided to reach the ileocecal and pyloric sphincters.
The small intestine was weighed down.
The small intestine's contents were gathered.
A graduated tube was used to collect the intestinal contents, and the volume was measured. The difference between the weights of the full and empty intestines was computed when the intestine was reweighed (Mabeku et al., 2006).

Enteropooling Assay

Animal Grouping and Treatment: Animals were randomly divided into six groups, each containing five rats. The various groups were treated as follows:
Group 1: Negative control (received distilled water)
Group 2: Positive control (received 2 ml of castor oil orally)
Groups 3-5: Test groups (received varying doses (300, 400, and 500 mg/kg BW) of *Prosopis farcta* L. fruit ethanolic extract)
Group 6: Standard drug group (received Loperamide 2.5 mg/kg body weight)

All treatments were administered orally and were followed by the administration of 2 ml of castor oil to induce enteropooling, except for the negative control group.

Enteropooling Induction: Two hours after treatment, enteropooling was induced in all groups except the negative control by administering 2 ml of castor oil orally. The method for inducing enteropooling follows the protocol described by (Mascolo et al., 1993).

Intestinal Fluid Accumulation Measurement: Two hours post-castor oil administration, the animals were sacrificed, and the small intestine was carefully dissected out from the pyloric sphincter to the ileocecal junction. The intestinal contents were collected, and the volume was measured using a graduated tube.

Weight Measurement: The small intestine was weighed before and after the removal of its contents.

Volume Measurement: The volume of the intestinal contents was measured and recorded.

Histopathological Analysis

After completion of treatment period, the animals were anesthetized using chloroform (by inhalation) and sacrificed by longitudinal dislocation. Collected organ were washed thoroughly with tap water to remove any race of blood. Fat tissues adhered to the organs were also removed carefully and afterwards organs were sliced into small tissue pieces using a surgical scalpel for allowing easy penetration of the chemicals inside the tissue. The dissected tissue was subsequently washed under running tap water until complete removal of most of the fluid from the tissues. The intestine was used as a sample in the histopathological study experiment for all groups. Then the intestine was obtained and put in a plastic container containing formalin solution (10%). Hematoxylin and eosin was used to stain the tissue for preparing permanent slide. Histopathological changes were observed under a light microscope (Mamun et al., 2014).

Statistical Analysis

Statistical analysis was performed using the SAS (2018) program. Data were subjected to one-way ANOV and the post-hoc Least Significant Difference (LSD) test was used for mean comparisons at P≤0.05 (SAS, 2018).

RESULTS

Prosopis farcta L. fruit extraction (by ethanol) and phytochemical analysis

Extraction: *Prosopis farcta* L. Fruits were extracted with ethanol 70% for 24 hours, yielding a dark brown extract with a semi-gelatinous and sticky texture. The extraction yield for *Prosopis farcta* L. fruits was 27% (Figure 1). The phytochemical analysis of the fruit extract from *Prosopis farcta* L. produced positive results for phenol, coumarins, terpenoids, resins, saponins, flavonoids, tannins and gly

Table 2: *Prosopis farcta* L. fruit ethanol extract chemical composition

No.	Type of test	Result
1	Tannins test	++
2	Carbohydrate test	+
3	Glycosides test	+
4	Phenols test	++
5	Resins test	++
6	Flavonoids test	+
7	Saponins test	+
8	Alkaloid test	+
9	Protein test	_
10	Coumarins test	+
11	Terpens test	+
12	Steroids test	_

Table 3: Effect of *Prosopis farcta* L. Fruit Extract on Rat Enteropooling Induced by Castor Oil

Group	Mean ± SE		
	Weight of intestine with content (g)	Weight of intestine empty (g)	The volume of intestine content (ml)
Negative Group	3.30 ±0.00 b	2.03 ±0.00 c	2.35±0.00 c
Positive control (induce diarrhea by castor oil)	4.89±0.00 b	3.17 ±0.00 bc	4.00 ±0.00 b
Castor oil and 300 mg \kg of *Prosopis farcta* L. fruits extract	7.89 ±0.81 a	3.83 ±0.08 ab	3.67 ±0.55 b
Castor oil and 400 mg\kg of *Prosopis farcta* L. fruits extract	10.45 ±0.72 a	4.76 ±0.21 ab	6.33 ±0.76 a
Castor oil and 500mg\kg of *Prosopis farcta* L. fruits extract	9.89 ±1.10 a	5.51 ±0.58 a	4.33 ±0.76 b
Castor oil and loperamide	9.94 ±0.77 a	5.29 ±0.08 a	4.67 ±0.56 b
LSD value	3.017 *	1.649 *	1.305 *

Means having with the different letters in same column differed significantly. * (P≤0.05).

cosides, alkaloids, and the absence of steroids or protein (Table 2).

Figure 1: Fruits of *Prosopis farcta* L. appearance in ethanolic extract.

Effect of *Prosopis farcta* L. Fruit Extract on Rat Enteropooling Induced by Castor Oil

Administration of castor oil resulted in the accumulation of intraluminal fluid within the gastrointestinal tract. This effect was significantly mitigated by the ethanolic extract of *Prosopis farcta* L. fruits at varying concentrations—300, 400, and 500 mg/kg BW—as well as at 2.5 mg/kg BW. Notably, a marked difference was observed in the size and weight of the intestinal contents among the six experimental groups ($P<0.05$). The group treated with the ethanolic extract at a concentration of 500 mg/kg BW showed the most substantial reduction in both the size and weight of the gut content when compared to other treatment groups (Table 3).

Histopathological Examination of the Intestine

Histopathological comparison of the duodenal layers in male rats from different treatment groups. Histopathlogical section of the duodenum for one rat in the first group

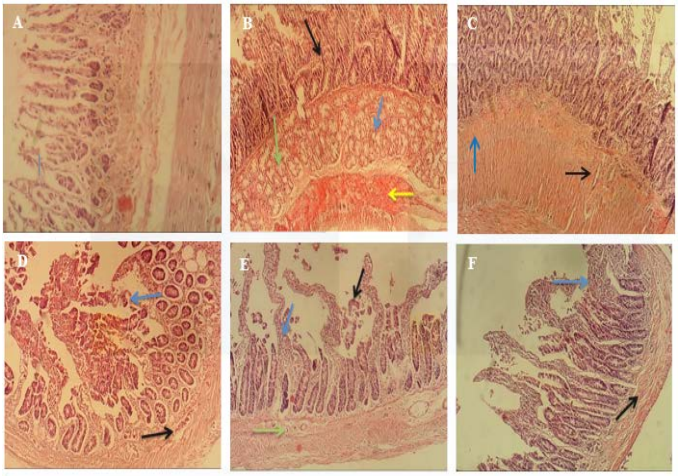

Figure 2: Histopathological comparison of the duodenal layers in male rats from different treatment groups (H&E stain 20×). A) Histopathlogical section of the duodenum for one rat in the first group (negative control) showing no abnormal lesion that each layers of mucosa, submucosa, muscularis and serosa give normal appearance. B) Histopathological section of the duodenum for one rat in the second group (positive control) showing thickening in each layers of duodenum and infiltration of infilammatory cells (Mononuclear cells) (Blue arrow) and hyper plastic proliferation of goblet cells (Black arrow) and glandular of sub mucosal (Green arrow) and thickening of muscular layer (Yellow arrow). C) Histopathological section of the duodenum for one rat in the third group (treated by *Prosopis farcta* L. fruits extract 300mg /kg.BW) Sub mucosa also showing infiltration of inflammatory cells (Blue arrow) with edema (Black arrow) and destruction of glands, muscularis showing thicking with slight infiltration of inflammatory cells and thickening of all layers. D) Histopathological section of the duodenum for one rat in the fifth group (treated by *Prosopis farcta* L. fruits extract 400mg /kg.BW) showing sloughing and infiltration of inflammatory cells of mucosa (Blue arrow) and sub mucosa slight edema in mucosa (Black arrow). E) Histopathological section of the duodenum for one rat in the fourth group (treated by *Prosopis farcta* L. fruits extract 500mg /kg.BW) All layers of this group showing slight lesion which involve infiltration of mono nuclear cells especially in mucosal layer (Blue arrow) with very little sloughing amount of epithelia lining mucosa (Black arrow) also slight edema and inflammatory cells in sub mucosa (Green arrow) with normal appearance of muscular layer. F) Histological section of the duodenum for one rat in the sixth group (treated by loperamide 2.5mg /kg.BW) showing sloughing and infiltration of inflammatory cells of mucosa (Blue arrow) and sub mucosa slight edema in mucosa (Black arrow).

(negative control) showing no abnormal lesion that each layers of mucosa, submucosa, muscularis and serosa give normal appearance (Figure 2A). Histopathological section of the duodenum for one rat in the second group (positive control) showing thickening in each layers of duodenum and infiltration of infilammatory cells (Mononuclear cells) and hyper plastic proliferation of goblet cells and glandular of sub mucosal and thickening of muscular layer (Figure 2B). Histopathological section of the duodenum for one rat in the third group (treated by *Prosopis farcta* L. fruits extract 300mg /kg.BW) Sub mucosa also showing infiltration of inflammatory cells with edema and destruction of glands, muscularis showing thicking with slight infiltration of inflammatory cells and thickening of all layers (Figure 2C). Histopathological section of the duodenum for one rat in the fifth group (treated by *Prosopis farcta* L. fruits extract 400mg /kg.BW) showing sloughing and infiltration of inflammatory cells of mucosa and sub mucosa slight edema in mucosa (Figure 2D). Histopathological section of the duodenum for one rat in the fourth group (treated by *Prosopis farcta* L. fruits extract 500mg /kg.BW) All layers of this group showing slight lesion which involve infiltration of mono nuclear cells especially in mucosal layer with very little sloughing amount of epithelia lining mucosa also slight edema and inflammatory cells in sub mucosa with normal appearance of muscular layer. (Figure 2E) Histological section of the duodenum for one rat in the sixth group (treated by loperamide 2.5mg /kg.BW) showing sloughing and infiltration of inflammatory cells of mucosa and sub mucosa slight edema in mucosa (Figure 2F).

DISCUSSION

Effect of *Prosopis farcta* L. Fruit Extract on Rat Enteropooling Induced by Castor Oil

By blocking the cystic fibrosis transmembrane conductance regulator or calcium-activated channels and generating protein-precipitating reactions to the gastrointestinal mucosa, the tannins in the extract may restrict fluid secretion (Hanafy et al., 2020). Flavonoids may lessen fluid secretion by blocking the release of acetylcholine (Najman et al., 2021). In the castor oil-induced enteropooling assay, the extract at all doses significantly decreased intraluminal fluid accumulation when compared to the negative control (Sarin et al., 2013). The extract's maximum efficacy was comparable to that of loperamide, one of the most commonly prescribed medications for diarrhea disorders, as demonstrated in the current investigation. Loperamide efficiently counteracted castor oil-induced diarrhea (Liu et al., 2014). It is therefore likely that the extract greatly reduces gastrointestinal hypersecretion and enteropooling by enhancing reabsorption of electrolytes and water or by preventing induced intestinal fluid buildup (Jahan et al., 2019).

Histopathological Examination of the Intestine

Similar findings were reported by (Babale et al, 2018), who demonstrated that albino Wistar rats subjected to 1 ml castor oil caused blunted villus tips and inflammatory cell infiltration. Moderate symptoms of intestinal disease (severe duodenal damage) (Freeman., 2009). Intestinal blockage variations in the quantity of goblet cells and the mucus they produce (Sethi and Smith., 2007). (Mohamed, 2008) *Prosopis farcta* L. fruit extracts are absorbed by the intestinal epithelium. The intestinal mucosa had severe necrotic and degenerative changes, according to the histological changes. Between the mucosa and the submucosa is edema (Hanna et al., 2005). By reducing villus height, increasing the number of goblet cells, and altering other team points, the current study proved that morphological alterations occurred in the wall and epithelial lining of the duodenum in rats (Trevizan et al., 2016). Disruptions to the metabolism and imbalances in the intestine brought on by the intestinal epithelium can result in inflammation and intestinal illness (Krausova et al., 2021).

CONCLUSION AND RECOMMENDATIONS

The current study has shown that an ethanolic extract from *Prosopis farcta* L. fruits has the potential to be an effective agent against secretory diarrhea that is induced by castor oil in rats. This was demonstrated by the findings of the present investigation. Not only did the extract exhibit significant antidiarrheal activity, but its efficacy was comparable to that of the antidiarrheal drug loperamide, which is widely prescribed for the treatment of diarrhea. In addition, a microscopic examination of the duodenal tissue revealed a decrease in the amount of mucosal epithelial sloughing, minimal edema, and a reduction in the amount of inflammatory cell infiltration in the submucosal layer. The normal appearance of the lining of the muscularis provides additional evidence that the extract has potential as a therapeutic agent. The implications of these findings for future research are extensive. Research moving forward should analyze the dose-response relationship of *Prosopis farcta* L. extract to determine its optimal therapeutic concentration. The extract's mechanism of action against diarrhea may be significantly aided by research into the molecular pathways involved in this effect. More research comparing *Prosopis farcta* L. to other antidiarrheal medications is necessary to bolster its scientific credibility. Consideration should also be given to determining the extract's long-term safety. Given the encouraging findings in rat models, it may be prudent to move forward with phase I and II clinical trials to confirm its safety and effectiveness in humans. Broadening the focus of the study to include multiple forms of diarrhea would yield more complete information about the extract's effectiveness. Finally, for quality control and standardization, it is essential to identify and quantify the bioactive compounds present in the extract.

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NOVELTY STATEMENT

The study's originality focuses on the ethanolic extract from Prosopis farcta L. fruits' histopathological and anti-secretory effects.

AUTHORS CONTRIBUTION

Contributions from each author were equal.

CONFLICT OF INTEREST

There are no competing interests of the authors.

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