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ANTIDIARRHOEAL ACTIVITY STUDIES OF *Ficus pumila* L. LEAF EXTRACT IN LABORATORY ANIMALS

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ABSTRACT

The objective of this study was to investigate the anti diarrhoeal activity of ethanolic extract of leaves of *Ficus pumila* L. (Moraceae) in experimental animals. Two doses (200 mg/kg and 400 mg/kg) of the extracts were used for the study. The experiments was performed by using two models such as castor oil induced model and magnesium sulphate induced model. Loperamide 3mg/kg was used as the standard drug. All drugs were administered by the oral route. The result showed that administration of the extract of *Ficus pumila* L. to the animals significantly decreases the number of faecal droppings and increases the percentage inhibition of defecation in a dose dependent manner. Phyto-chemical analysis revealed the presence of carbohydrate, glycosides, sterols, flavonoids and triterpenes. From the results obtained it could be concluded that the ethanolic extract of leaves of *Ficus pumila* L. possess significant, dose dependent antidiarrhoeal activity.

KEYWORDS

Ficus pumila L., Antidiarrhoeal activity, Castor oil, Magnesium sulphate, Loperamide.

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INTRODUCTION

Diarrhoea is a common medical condition that is characterized by increased frequency of bowel movements and increased liquidity of stool[1]. WHO define diarrhoea as the passage of three or more loose stools in a 24 h period. Although acute diarrhoea is typically self-limiting, it can be severe and can lead to profound dehydration, which can lead to abnormally low blood volume, low blood pressure, and damage to the kidneys, heart, liver, brain and other organs. Acute diarrhoea remains a major cause of infant mortality around the world. Over 2 million deaths are attributed to acute diarrhoea each year world-wide, most of them in the

developing world. Children and the elderly are particularly prone to dehydration secondary to diarrhoea[2]. Diarrhoea is a common symptom of gastrointestinal infections caused by a wide range of pathogens, including bacteria, viruses and protozoa. However, just a handful of organisms are responsible for most acute cases of diarrhoea. Rotavirus is the leading cause of acute diarrhoea, and is responsible for about 40 per cent of all hospital admissions due to diarrhoea among children .Other major bacterial pathogens include E. coli, Shigella, Campylobacter and Salmonella, along with V.cholera during epidemics. Cryptosporidium has been the most frequently isolated protozoan pathogen among children seen at health facilities and is frequently found among HIV-positive patients. Though cholera is often thought of as a major cause of child deaths due to diarrhoea, most cases occur among adults and older children[3].

There are three main forms of acute childhood diarrhoea, all of which are potentially life-threatening and require different treatment courses: a) Acute watery diarrhoea, includes cholera and is associated with significant fluid loss and rapid dehydration in an infected individual. It usually lasts for several hours or days. The pathogens that generally cause acute watery diarrhoea include V. cholerae or E. coli bacteria, as well as rotavirus.b) Bloody diarrhoea, often referred to as dysentery, is marked by visible blood in the stools. It is associated with intestinal damage and nutrient losses in an infected individual. The most common cause of bloody diarrhoea is Shigella, a bacterial agent that is also the most familiar cause of severe cases and c) Persistent diarrhoea is an episode of diarrhoea, with or without blood that lasts at least 14 days. Undernourished children and those with other illnesses, such as AIDS, are more likely to develop persistent diarrhoea. Diarrhoea, in turn, tends to worsen their condition. Four general pathophysiologic mechanisms disturb water and electrolyte balance, leading to diarrhoea are (a) An alteration in active ion transport by either decreased sodium absorption or increased chloride secretion; (b) change in intestinal motility; (c) increase in luminal osmolarity; and (d) increase in tissue hydrostatic pressure. These mechanisms have been related to four broad clinical diarrheal groups: secretory, osmotic, exudative, and altered intestinal transit[4].

According to World Health Organization (WHO) about 80% of the world's populations mainly depend on traditional medicine and the use of plant extract is mainly involved in the traditional treatment[5]. Medicinal plants constitute the major component of the traditional medicine practiced worldwide due to the economical viability, accessibility and ancestral experience[6]. Herbal medicine is fast emerging as an alternative treatment to synthetic drugs for treatment of most diseases possibly due to lower costs, availability, fewer adverse effects and perceived effectiveness and plants are more potent healers because they promote the repair mechanisms in the natural way[7]. Therefore, the search for safe and more effective agent from plant origin has continued to be an important area of active research. Hence, the World Health Organization encouraged studies for the treatment and prevention of diarrhoeal diseases depending on traditional medical practices[8].

In the present study a plant from the Genus *Ficus*, named *Ficus pumila* L. of the Moraceae family was selected, which is a scandent shrub with evergreen coriaceous leaves that is normally grown between the trees as well as on fragmented surface. The leaves of the plant has been traditionally consumed by some Okinawan elders either as a beverage or used as an invaluable medicinal herb by the folks to treat diabetes, dizziness, high blood pressure, and neuralgia[9,10]. Several studies have been performed on the composition of *Ficus pumila* L. and phytochemical analysis was performed and confirmed the presence of carbohydrate, glycosides, sterols, flavonoids and triterpenes. The important constituents isolated in the previous study were apigenin, luteolin, rutin, genistein, hesperidin, astragalin, isoquercitrin, and chrysin[11]. Although many other species of this genus such as Ficus *racemosa Linn*[12], *Ficus benghalensis*[13], *Ficus hispida*[14], *Ficus religiosa*[15], *Ficus carica*[16], *Ficus exasperate*[17], *Ficus trichopoda*[18], *Ficus Benjamina*

'Variegata[19] has been reported for antidiarrhoeal activity. However, the antidiarrhoeal activity of *Ficus pumila* L. had never been investigated, thus the present study was initiated to evaluate the anitdiarrhoeal activity of ethanolic extract of leaves of *Ficus pumila* L. in experimental animals.

MATERIALS AND METHOD

Collection of Plant material and preparation of extract

The leaves of *Ficus pumila* L. were collected from the campus of Nandha college institution- Erode (Tamilnadu). The plant was identified and authenticated by Botanical Survey of India, Tamilnadu Agricultural University Campus (TNAU), Coimbatore. The voucher specimen (BSI/SRC/5/23/2012-13/Tech-448) has been deposited in the herbarium of TNAU for future reference. The leaves were shade dried, powdered and were extracted using 70% ethanol as the solvent in a soxhlet apparatus until complete extraction. Solvent evaporation under reduced pressure was carried out to get semisolid extract which was used for the studies.

Experimental animal

The study was conducted on Wistar Albino rats of 150 – 200 g maintained under standard conditions (room temperature 24^0C- 27^0C and humidity 60 – 65 %). The food in the form of dry pellets (M/s Hindustan Lever Foods, Bangalore) and water were available *ad libitum*. Rats of either sex were selected and grouped in to four having 6 animals each. All the experimental procedures and protocols used in this study were reviewed by the Institutional Animal Ethics committee (688/2/C-CPCSEA) of NCP and were in accordance with the guidelines of the IAEC. Approval was obtained from IAEC, NCP (Proposal No- NCP / IAEC / No: 9/2012-13).

The animals were divided into four groups, each containing six each. Group I was served as solvent control and received 0.5% CMC (10 ml/kg). Group II treated as positive control was received Loperamide (3 mg/kg). Group III and IV were received ethanolic extract of Ficus pumila L. 200mg/kg and 400 mg/kg respectively. All the treatments were administered orally 60 min prior to start the experiment.

Phytochemical screening

The freshly prepared crude ethanolic extract of *Ficus pumila* L. was qualitatively tested for the presence of major phytochemical constituents according to standard methods[20].

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Castor oil induced diarrhoea[21]

Rats fasted for 24 h were randomly allocated to four groups of six animals each. Group 1 received 0.5 % carboxy methyl cellulose (CMC, 10ml/kg), group2 and group 3 received 200 and 400mg/kg of ethanolic extract of *F.pumila* L. respectively and group 4 was given loperamide (3mg/kg) in oral routs. After 60 min each animal was given with 2 ml of castor oil by gastric intubation, each animal was placed in an individual cage, the floor of which was lined with blotting paper which was changed every hour, observed for 4 h and the characteristic diarrhoeal droppings were recorded.

The percentage inhibition can be determined by using the following equation

$$\mathrm{PI} = \frac{\text{mean defecation(control} - \text{treated groups)}}{\text{mean ulcer defecation(control group)}} \times 100$$

Magnesium sulphate induced diarrhoea[22]

The rats are fasted overnight and placed in the individual cages, the floor of which will be lined with blotting paper. They will be randomly allocated to four groups of six animals each. Group I will receive the vehicle orally (0.5% CMC 10ml/kg), group II will be given Loperamide (3 mg/kg, p.o.), group III and group IV will receive ethanolic extract of Ficus *pumila* L. at a dose 200mg/kg and 400mg/kg respectively. All the drugs are given by oral routs. After 30 min, each animal will be given 2 gm/kg of magnesium sulphate (p.o.). The animals are then observed for 4 hours and the characteristic diarrhoeal droppings are recorded. The other parameter to be noted was percentage inhibition of diarrhoea.

RESULTS

Phytochemical analysis

The phytohemical analysis of the ethanolic extract of *F. pumila* L. revealed the presence of carbohydrate, glycosides, sterols, flavonoids and triterpenes.

Castor oil induced diarrhoea

The ethanolic extract of *Ficus pumila* L. leaves exhibited significant antidiarrhoeal activity against castor-oil challenged diarrhoea in rats. The extract showed marked reduction in the frequency of defecation, fecal droppings and percentage protection of diarrhoea when compared to control group. The extract at a dose of 400 mg/kg had shown more significant effect when compared to the standard drug loperamide (Figure No.1). The results are given in the Table No.1.

Magnesium sulphate induced diarrhoea

Ethanolic extract of *Ficus pumila* L. elicited a dose dependent activity against magnesium sulphate induced diarrhoea. The extract (400mg/kg) provided maximum percentage of protection (73.73%) against diarrhoea induced by magnesium sulphate as compared to the standard drug (loperamide, 3mg/kg) (Figure No.2). The extract at 200mg/kg produces a protection of 46.34% and the values are given in the Table No.2.

DISCUSSION

The aim of the present study was to assess the effect of ethanolic extract of *Ficus pumila L*. on diarrhoea .Diarrhoea results from an imbalance between the absorptive and secretary mechanisms in the intestinal tract, which is accompanied by an excess loss of fluid in the faeces. In some types of diarrhoea, the secretary component predominates, while other types of diarrhoea are characterized by hyper motility. Several mechanisms have been previously proposed to explain the diarrheal effect of castor oil including inhibition of intestinal Na+, K+-ATPase activity to reduce normal fluid absorption[23], activation of adenylate cyclase or mucosal cAMP mediated active secretion[24], stimulation of prostaglandin formation[25], platelet activating factor and recently nitric oxide has been claimed to contribute to the diarrheal effect of castor oil[26]. However, it is well evident that castor oil produces diarrhoea due to its most active component recinoleic acid[27] which stimulates the peristaltic activity in the small intestine, leading to changes in the electrolyte permeability of the intestinal mucosa. Its action stimulates the release of endogenous prostaglandins [25]. In this study, the result reveals that the ethanolic extract of *Ficus pumila* L. exhibited a significant anti diarrhoeal activity. Earlier studies have shown that the presence of phytoconstituents such as flavonoids, sterols and/or tri terpenes having anti diarrhoeal properties[28]. This may be due to the fact that the extract increases the re absorption of water from the intestine. Loperamide, a drug widely used in the management of diarrhoea disorders was reported to be effective in the prevention of diarrhoea induced by castor oil, prostaglandins, and cholera toxin[29]. The pharmacological effect of loperamide is due to its anti-motility and anti-secretory properties[30]. From our investigation, it is likely that the plant extracts mediate their effects through similar mechanisms. Prostaglandins are implicated in the patho-physiology of diarrhea[31]. Flavonoids are known to modify the production of cyclooxygenase 1 and 2 (COX-1, COX-2) and lipo-oxygenase (LOX) there by inhibiting prostaglandin production[32]. The activation of LOX is induced by fatty meals while COX1and COX-2 is by diarrhoea-genic agents. Though several constituents are present in the extracts, it is most likely that flavonoids, singly or possibly other constituents, are responsible for the observed anti-diarrhoea effects of *Ficus pumila L.*

Magnesium sulphate produces the diarrhoea by osmotic properties, preventing reabsorption of water ions, leading to increase in the volume of the intestinal content. It promotes the liberation of cholecytokinin from the duodenal mucosa, which increases the secretion and motility of small intestine and thereby prevents the reabsorption of sodium chloride and water[33]. The ethanolic extract of *Ficus pumila* L. Found to reduce the diarrhoeic condition in this model. *Ficus pumila* L (Figure No.3). May have increased the absorption of water and electrolyte from the gastrointestinal tract.

Table No.1: Effect of ethanolic extract of *Ficus pumila* L. on castor oil induced diarrhoea

S.No	Groups	Treatment	No. of faecal dropping in 4 hours	%inhibition of defecation
1	1 (Control)	0.5% CMC(10ml/kg) (1ml/kg)	10.6 ±0.60	_
2	2 (Standard)	Loperamide(3mg/kg)	1.2± 0.20**	88.68
3	3	Extract of F.pumila (200mg/kg)	7.2± 0.37**	32.08
4	4	Extract of F.pumila (400mg/kg)	4.2± 0.37**	60.37

(Results are mean ± S.E.M; (n = 6) Statistical comparison was performed by using ANOVA followed by Dunnet't' test. * P < 0.05, **P < 0.01, ***P < 0.001 were consider statistically significant when compared to control group.)

Table No.2: Effect of ethanolic extract of *Ficus pumila* L. on magnesium sulphate induced diarrhoea

S.No	Groups	Treatment	No. of faecal dropping in 4 hours	%inhibition of defecation
1	1 (Control)	Normal saline (1ml/kg)	8.2 ±0.37	_
2	2 (Standard)	Loperamide(3mg/kg)	1.2 ±0.20**	85.37
3	3	Extract of F.pumila (200mg/kg)	4.4± 0.40**	46.34
4	4	Extract of F.pumila (400mg/kg)	2.4± 0.24**	70.73

(Results are mean ± S.E.M; (n = 6) Statistical comparison was performed by using ANOVA followed by Dunnet't' test. * P < 0.05, **P < 0.01, ***P < 0.001 were consider statistically significant when compared to control group.)

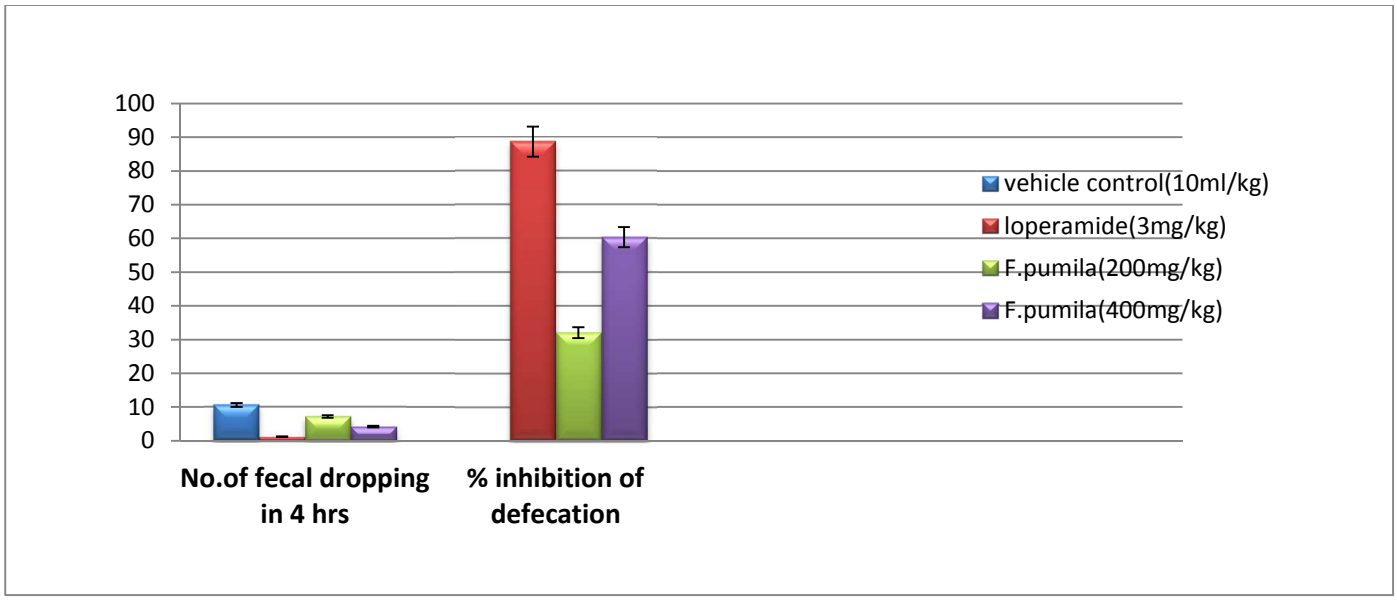

Figure No.1: Effect of ethanolic extract of *Ficus pumila* L. on castor-oil induced diarrhoea in rats

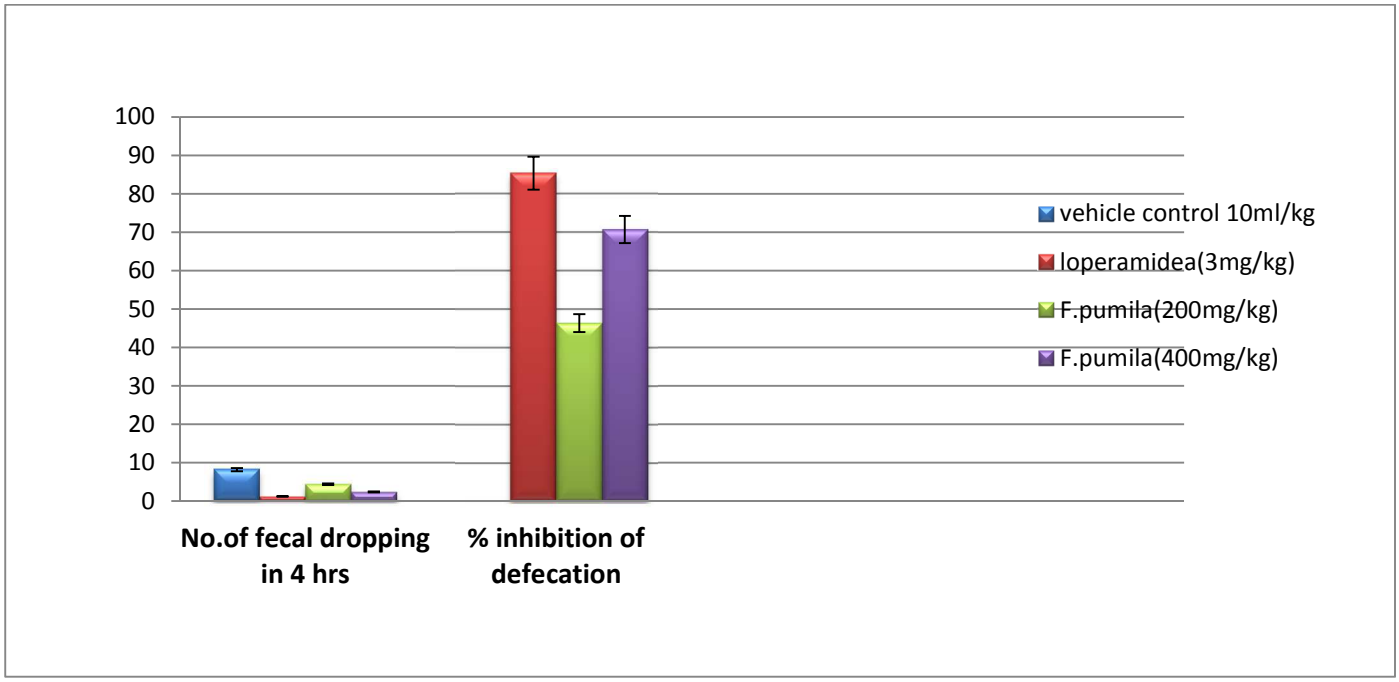

Figure No.2: Effect of ethanolic extract of *Ficus pumila* L. on magnesium sulphate induced diarrhoea in rats

Figure No.3: Photograph of *Ficus pumila L. showing fruits and leaves*

CONCLUSION

The remarkable anti-diarrhoeal effect of *Ficus pumila L.* leaf extract against castor oil and magnesium sulphate induced diarrhoea models attests to its utility in a wide range of acute diarrhoeal states. On the basis of these findings, it can be assumed that leaves of *Ficus pumila L.* could be a potential source for novel 'lead' discovery for antidiarrhoeal drug development. Although the investigated plant may be useful in a wide range of diarrhoeal states; further studies are needed to completely understand the mechanism of anti-diarrhoeal action of *Ficus pumila L.* leaves.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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