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Evaluation of phytochemical screening, acute toxicity and *in vivo* anti-diarrheal activity of *Ehretia serrata* Roxb. and *Ehretia obtusifolia* Hocht. Ex.A.DC. Family Boraginaceae

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Ehretia serrata and *Ehretia obtusifolia* are utilized for hundreds of years in several countries ancient system of medication for the treatment of various diseases. The methanolic extracts of leaf, stem bark and fruit of each plants were found non-toxic against Balb/c mice. Medication effects of methanolic extract of leaf, fruit and stem bark of each plants tested against Balb/c mice by victimisation 2 models. In purgative (CO) evoked looseness of the bowels model, all 3 components of each plants showed extremely important (0.01) results at most dose level and reduced onset of looseness of the bowels, total and wet feculent output and average weight of total and wet excreta. In CO evoked gi motility model methanolic extract of *E. serrata* stem bark showed extremely important (0.01) results at dose level of 200mgkg and 300mg/kg. *E. obtusifolia* causes higher relaxation of the sleek muscles at terribly low concentrations and showed important results at lower dose level. Each leaf and stem bark showed extremely important results (0.01) at 200mg/kg and 300mg/kg doses, therefore providing a scientific proof for its ethno medical specialty utilize as a medication drug. The current study has discovered the various medicative properties of each plant will be exploited for therapeutic preparations on industrial scale.

Keywords: *Ehretia serrata*, *Ehretia obtusifolia*, Boraginaceae, diarrhea, phytochemical screening

INTRODUCTION

Plants are vital constituent of the universe and folks have used plants as medicines from the terribly starting. Plants have perpetually been a valuable supply medication of medicine and plenty of the presently out their drugs are derived directly or indirectly from them (Kahrizi et al. 2012). Totally different medications are synthesized from medicative plants. These medications are used as laxatives, blood thinners, antibiotics and anti-malaria are of plant origin. Taxol, periwinkle plant derivative and painkiller, that are acknowledge medications, are obtained from isolated from herb, periwinkle, yew and controlled substance

severally (Hassan, 2012). In past the plants extracts were used for natural process varied diseases (Van-Wyk and Wink, 2017). Presently, up to five hundredth of all medicines obtained from the extracts of various plants (Cragg and Newman, 2005). Borage family includes a hundred genera and 2000 species that are scattered in temperate regions of the globe, most significantly in Mediterranean and tropical regions. By comparison with alternative families the Boraginaceae thought of very cheap ranking families, containing few species of medicative price (Khan et al. 2011). There are varied plants famed for natural process of the many diseases all told over the globe. A number of the species of family Boraginceae are tested for isolation and characterization of varied chemical constituents like pyrrolizidine alkaloids, naphthaquinones, flavonoids, terpenoids, triterpenoids and phenols (Torane et al. 2010). A number of plant species of Boraginaceae are used as antimicrobial, antitumor, antiviral, anti-inflammatory drug, cardio tonic, contraceptive, antiplatelet, wound healing and autocoid restrictive (Sharma, 2009). *Ehretia serrata* Roxb. is native species to Asian country and Islamic Republic of Pakistan (Nasir, 1989).In Islamic Republic of Pakistan *Ehretia serrata* Roxb. is well distributed in sub-Himalayan tract from Azad geographical region westward to urban center, Islamabad, Murree, Hazara, and Swat. It's been with success planted in areas around city (Sheikh, 1993). *Ehretia obtusifolia* happens in the majority countries of eastern and southern Africa and in Madagascar.It extends into Asia up to Islamic Republic of Pakistan and Northwest Asian country (Schmelzer et al. 2008).

Loose of watery stool infection in gastro viscus tract is termed symptom. It's a dangerous malady and ratios of death because of this malady are chiefly 4-9 million each year worldwide. This malady affects all kinds of sex all told sort of conditions (Suleiman et al. 2008; Suleiman et al. 2015). Chiefly symptom is caused by unhealthy and insanitary water similarly as poor and contaminated surroundings. Newborns children's and tiny children principally at the age below seven are greatly affected (Yakubu and Salimon, 2015).Artificial drug like Diphenoxylate, Loperamide and antibiotics etc., are used however, these medication have several aspect effects.

Within the current investigation the acute toxicity, preliminary phytochemical screening and medicament potential of *Ehretia serrata* and *Ehretia obtusifolia* are evaluated, to rationalize its ancient uses as anti- diarrhoetic agent.

MATERIALS AND METHODS

Plant Materials

Fresh aerial components of *Ehretia serrata* and *Ehretia obtusifolia* were collected from Department of Botany, University of Peshawar in March 2016, and identified with the help of Flora of Pakistan by a Taxonomist faculty member, Prof. Dr. Abdur Rashid Department of Botany University of Peshawar, Pakistan. A voucher specimen was deposited within the Herbarium, Department of Botany University of Peshawar for additional reference.

Preparation of plant extract

The aerial components were dried at temperature and fine. As 1000g of dried powder of leaf, fruit and stem bark of each plant were marinated for seven days in 6000ml fuel discretely in spherical bottom flask. The flasks were sporadically jolted so as to expedite and consummate extraction procedure. The extract of every half was filtered and so the solvents were gaseous through rotary evaporator. The extracts were then keep in closed instrumentation in white goods for additional use.

Anti-diarrheal activity

Requirements

Balb/C mice of both sexes (18-24g), plant sample extracts, charcoal, ruler, normal saline water, feeding tubes, syringes and standard drug (Loperamide).

Animals

Colony bred Balb/C from Veterinary analysis Institute, Peshawar, were used within the study. The animals were unbroken in polypropene cages and underneath stable atmosphere and victuals with free access to Purina chow and clean drinking dihydrogen oxide at temperature, 24 ± 21^0C, and 50–55% relative hot weather. The animals were handled in accordance with the present pointers for the care of laboratory animals (National analysis Council, 2011).

Acute toxicity

Acute pharmacological medicine check was done of *Ehretia serrata* and *Ehretia obtusfolia* leaves, fruits and stem bark methanolic extract by utilizing Balb/C mice by following the quality technique of Baliga et al. (2004). Before beginning

experiment, Swiss anomaly mice were purchased for Veterinary analysis institute Peshawar and allow them to prompt by not giving the aliment and water for twelve hours. After twelve hours all mice were divided into nineteen teams, every cluster with 3 replicates. cluster one was taken as positive management cluster and treated with mundane saline water whereas The remaining eighteen was treated with leaf, fruit, and stem bark methanolic extract of *Eherta serrata* and *Ehretia obtusifolia* with doses of a hundred, 200mg/kg and 300mg/kg of weight through intraperitoneal injections. The results weren't negative. Neither pharmacological medicine symptoms were detected in every cluster nor any behavioral modification descried in any cluster of treated mice. The symptoms were ascertained for up to six hours. Next the dose was incremented up to 1000mg/kg and so 2000mg/kg body weights of the mice however no hepatotoxic symptoms and death was detected for successive twelve hour.

Castor oil (CO) induced diarrhoea

The method followed by Awouters et al. (1978) was used for this study. Balb/C mice of either sex were fasted for eighteen h and were classified into twenty teams of 3 animals every for all 3 components of each plants (100mg/kg, 200mg/kg and 300mg/kg). All teams were treated by mistreatment oral feeding for receiving indefinite quantity. The primary 2 teams were taken as a negative management (distilled water of ten ml/kg) and positive management (Loperamide three mg/kg). Remaining eighteen teams were taken as check cluster for 6 components (leaf, fruit and stem bark) of each experimented plants. For the methanolic extract, the dose levels of check teams were determined supported the acute toxicity check (Jitendra et al., 2011) (100 mg/kg, two hundred mg/kg and three hundred mg/kg). once one hour of doses administrations and treatment all animals received zero. 5 ml of CO, and so placed them in cages separately with study lined floor. Throughout four hour amount of observations, the onset of symptom, frequency of excreting and also the weight of feculent output (wet and total excretory product in gram) were recorded for individual mouse. The diarrhetic inhibition percentages of weight of feculent output were determined by following 1–3 formulae.

$$\% \text{ Inhibition} = \frac{\text{Average number of WFC} - \text{Average number of WFT}}{\text{Average number of WFC}} \times 100$$

Where, WFC = wet faeces in the control; WFT = wet faeces in the test group

$$\% \text{ Wet faecal output} = \frac{\text{Mean weight of wet faeces of each test group}}{\text{Mean weight of Wet faeces of control}} \times 100$$

$$\% \text{ Total faecal output} = \frac{\text{Mean weight of total faeces of each test group}}{\text{Mean weight of total faeces of control}} \times 100$$

CO induced gastrointestinal motility

This is a typical methodology to utilize for checking the extract efficiency on canal conveyance in mice. The nightlong fasted animals were first divided into twenty teams. The cluster one received traditional saline water intra-peritoneally (1cc= ten ml/kg) thought of as negative management, and loperamide drug (3mg/kg) were injected to cluster a pair of and regarded it as positive management cluster. Remaining eighteen teams used for every plant extract with concentration a hundred, one hundred fifty and 200mg/kg. Triplicates were used in every experiment. Animals were unbroken fixed nightlong. Twenty-five mints later when indefinite quantity all the animals were aliment with charcoal nutrition through victualing tubes and followed by death of those mice when half-hour through cervical dislocation and compound them (ethically approved) (Akanji and Yakubu, 2000; Gerald et al. 2007; Yakubu and Salimon, 2015).After dissection minuscule gut was abstracted. The gap traveled by the charcoal meal through gut was thought of because the share of the entire length of gut in line with the subsequent formula.

$$\% \text{ Intestinal transportation} = \frac{\text{Distance travelled by charcoal meal (cm)}}{\text{Total length of small intestine (cm)}} \times 100$$

***In vivo* antidiarrheal index**

In vivo antidiarrheal index (ADI) of positive control and extract treated group was determined by using different data from the above tests using the formula developed by Than et al., 1989; Robert et al. 1976.

$$\text{ADI In vivo} = D_{freq} \times G_{meq} \times P_{freq}$$

$$D_{refq} = \frac{\text{mean onset of diarrhea in the test group - mean onset of diarrhea in the control group}}{\text{mean onset of diarrhea in the control group}} \times 100$$

Gmeq is the gut meal travel reduction (as % of control) obtained from charcoal meal test (% inhibition), and Pfreq is the purging frequency or

reduction in the number of wet stools (as % of control) obtained from castor oil diarrheal model (% inhibition of defecation).

Statistical analysis

Statistical analysis of information was done through unidirectional ANOVA by SPSS (22) laptop computer code, Denotes + SEM were calculated through Microsoft surpass, Dunnet check were used for comparison between management and tested treatments. The likelihood likelihood.05 was thought-about vital and P≤0.01 thought-about extremely vital.

Preliminary phytochemical screening

The methanolic extracts of *Ehretia serrata* and *Ehretia obtusifolia* (leaves, fruit, stem bark) were tested for the presence of alkaloids, flavonoids, tannins, terpenoids, steroids, glycosides and saponins victimization commonplace chemical tests (Zohra et al.2012).

RESULTS

Acute toxicity

No pharmacological medicine symptoms were detected all told the clusters; neither any behavioral amendment was noticed in any group of treated mice once half dozen hours. Next the dose was inflated up to 1000mg/kg and so 2000mg/kg body weights of the mice however no nephrotoxic symptoms and death was detected for succeeding twelve hours. This established the non-toxic nature of *Ehretia serrata* and *Ehretia obtusifolia* extract and unconcealed the safe nature of those crude medications for human consumption and preparation of medication. The chosen most effective dose suggests each plants have a broader index and LD50 price bigger than 2000 mg/kg in mice.

Effect of ME (leaf, fruit and stem bark) of *Ehretia serrata* on purgative elicited diarrheic model within the CO-induced diarrheic model

The methanolic extract of *Ehretia serrata* leaf, fruit and stem bark prolonged the beginning of looseness of the bowels and reduced the prevalence of looseness of the bowels considerably with relevancy management. Average weight of wet and total soiled outputs was considerably (P≤0.05 vs. saline group) and extremely considerably (P≤0.01 vs. saline group) reduced at doses of two hundred mg/kg and three hundred mg/kg, once treated with methanolic extract of leaves as compared to manage. The one hundred mg/kg of the extract, however, showed a statistically non-significant result on frequency of wet BM (P ≤0.05 vs. saline group), weight of wet (P ≤ zero.05 vs. saline group) and total (P≤ zero.05 vs. saline group) soiled outputs. Besides, the information shows, methanolic extract of leaf exhibit share of diarrheic inhibitions fifty four 61% (P≤ 0.05 vs. saline group), 62.62% (p≤ 0.01), and 68.30% (P ≤ 0.01 vs. saline group) at the doses of one hundred mg/kg, 200 mg/kg, and four hundred mg/kg, respectively (Tab. 1).

Coming back to methanolic extract of fruit and stem bark, each created an extremely vital delay in initiation of looseness of the bowels at four hundred mg/kg (P ≤0.01 vs. saline group). The fruit extract considerably (P ≤ 0.05 vs. saline group) scale back each average weight of wet and total BM at 200mg/kg and manufacture extremely vital (P ≤0.01 vs. saline group) reduction at three hundred mg/kg. % inhibition showed by fruit metanolic extract was thirty five.33% (P≤0.05 vs. saline group), 48.13% (P ≤ 0.05 vs. saline group) and fifty nine.48 % (P ≤0.01 vs. saline group) in any respect 3 doses (100mg/kg, 200mg/kg and 300mg/kg). The stem bark additionally showed a big reduction in weight of each wet and total soiled outputs at two hundred mg/kg (P ≤0.05 vs. saline group) and three hundred mg/kg (P ≤0.01 vs. saline group) severally with the best share of diarrheic inhibition (65.80%, P ≤0.01 vs. saline group) obtained at three hundred mg/kg followed by forty nine.59% at two hundred mg/kg and thirty five.17% at one hundred mg/kg. On the contrary, the stems bark considerably delays in onset of looseness of the bowels in any respect tested doses as compared with management (Tab. 1). There was a dose-dependent reduction within the share of weight of wet and total soiled outputs showed by methanolic extract of all 3 components *Ehretia serrata* (Fig. 1).

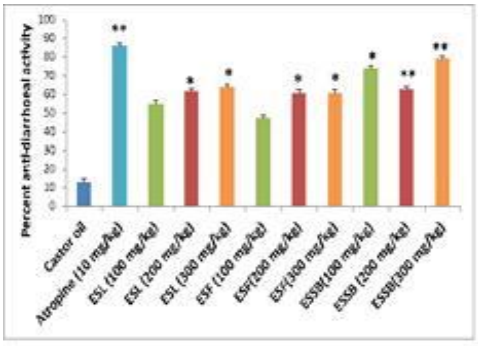

FIGURE 1 - Percent anti-diarrhoeal activity of *E. serrata*

Table 1: Effect of the methanolic leaf, fruit and stem extracts of *Ehretia serrata* on castor oil induced gastrointestinal transit in mice

	Dose (mg/kg)	Onset of diarrhea (Min)	No of wet faeces	Total No of faeces	Average weight of wet faeces (gm)	Average weight of total faeces (gm)	% Inhibition of defecation	% WWFO	% WTFO
Control		78.55±7.99	6.17±0.33	6.8±0.49	0.37±0.02	0.38±0.02			
Loper amide		178.50±19.80**	1.79±0.39**	2.73±0.59**	0.09±0.02**	0.11±0.02**	70.98	24.32	28.94
Leaves	100	135.67±15.17*	2.80±0.89	3.50±0.72*	0.18±0.02	0.21±0.02	54.61	48.64	55.26
	200	148.00±22.80**	2.30±0.50*	3.00±0.67**	0.13±0.03**	0.16±0.06*	62.62	35.13	42.10
	300	176.83±19.30**	1.95±0.49**	2.50±0.89**	0.11±0.09**	0.12±0.02**	68.30	29.79	31.57
Fruit	100	120.12±24.81	3.99±1.23	4.48±1.08	0.21±0.05	0.22±0.06	35.33	56.75	57.89
	200	138.50±21.90*	3.20±0.68*	4.67±0.76	0.16±0.02*	0.17±0.07*	48.13	43.24	44.72
	300	157.00±19.01**	2.50±0.79*	3.17±0.83*	0.13±0.04**	0.14±0.06**	59.48	27.02	36.84
Stem bark	100	110.33±18.14	4.00±0.40	5.67±0.41	0.22±0.04	0.24±0.08	35.17	59.45	63.15
	200	125.00±29.01*	3.13±0.87*	4.03±1.05	0.18±0.09*	0.20±0.05	49.59	48.64	52.83
	300	165.50±24.00**	2.11±0.98**	3.50±1.23*	0.14±0.07**	0.13±0.08**	65.80	37.83	34.21

The data of castor oil induced gastrointestinal transit in mice of *Ehretia serrata* are reported as mean ± SEM (n=5) and were analysed through ANOVA following Dunnett's post-hoc, compared to control values, significant at *P≤0.05 and highly significant at **P≤0.01.

Effect of ME (leaf, fruit and stem bark) of *Ehretia obtusifolia* on castor oil induced diarrheal model

Castor oil administration to mice elicited diarrhea for the subsequent four hr within the management and take a look at teams. Loperamide (78.50%) markedly low-impact inhibition of excretion moreover because the extracts scale back its considerably too, most impact (P≤0.01 vs. saline group) were seen at dose level three hundred mg/kg altogether 3 elements (69.81%, leaf; 68.81%, fruit and seventy.01%, stem bark) of *Ehretia obtusifolia* as shown in Tab. 2. A share of average weight of wet fecal output and total fecal output showed by all 3 elements (leaf, fruit and stem bark) were markedly (P≤0.01 vs. saline group) reduced at higher doses (300mg/kg), compared to manage moreover as onset of looseness of the bowels with the upper dose (200mg/kg, P≤0.05 vs. saline group; three hundred mg/kg, P≤0.01 vs. saline group) of the extract showed the higher impact. All elements at 200mg/kg doses of the extract reduced considerably (P≤0.05 vs. saline group) reciprocal inhibition with the utmost impact (55.50%) showed by leaf, followed by fruit (54.64%) so by stem bark (53.64%). Oral pre-treatment of mice with completely different doses of the extract showed a extremely vital (P≤0.01 vs. saline group) delay on the onset of diarrhea, with the upper dose of the extract. The frequency of excretion and amount of wet and total stool become considerably (P≤0.01 vs. saline group) reduced with regard to management at higher doses (200mg/kg, 300mg/kg). Additionally, the extract considerably (P≤0.01 vs. saline group) reduced the frequency of excretion, the quantity of wet and total stools once examination with management (P≤0.01vs. saline group), particularly at high doses (200mg/kg; 300mg/kg). Share of fecal output was non-significant (P≤0.05 vs. saline group) at low dose levels (100mg/kg) nearly altogether elements of experimented elements (Tab. 2; Fig. 2).

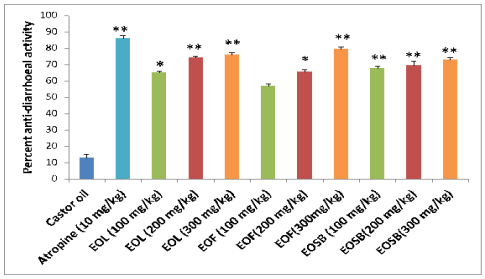

FIGURE 2- Percent anti-diarrhoeal activity of *E. obtusifolia*

The data of castor oil induced gastrointestinal transit in mice of *Ehretia obtusifolia* are reported as mean ± SEM (n=5) and were analyzed through ANOVA following Dunnett's post-hoc, compared to control values, significant at *p≤0.05 and highly and highly significant at **p≤0.01.

Effect of Methanolic extract of leaf, fruit and stem bark of *Ehretia serrata* on gastrointestinal motility

In the present bioassay the medicinal drug efficiency of leaf methanolic extract of *Ehretia serrata* was tested, and its results disclosed that there have been internal organ conveyance of charcoal were forty five.1%, 38.5% and 36.5% with mean values twenty six.000±0.57735, 22.3367±0.33168, 20.7667±0.23333 at dose level 100mg/kg, 200mg/kg and three hundred mg/kg weight severally. The unidirectional ANOVA showed methanolic extract of leaf of *E. serrata* was predominate (P≤0.05 vs. saline group) in the slightest degree doses (100mg/kg, 200mg/kg and 300mg/kg). The medicinal drug efficiency of fruit of methanolic extract additionally tested and gets vital results (P≤0.05 vs. saline group) at higher doses (200mg/kg and three hundred mg/kg). Methanolic fruit extract showed that there have been internal organ transportation of charcoal were fifty two.64, 39.26, 39.5 you bored with mean values thirty.0300±2.50484, 22.7333±5.62178, 23.7000±4.97226 at 3 dose levels 100mg/kg, 200mg/kg and three hundred mg/kg weight severally. Same as leaf and fruit extract, stem bark of experimented plant were in addition tested and results were extremely predominate (P≤0.01 vs. saline group) at 200mg/kg and three hundred mg/kg and important at 100mg/kg compared to traditional saline (87%) and loperamide (14%). Stem bark showed vital (P≤0.05 vs. saline group) nada internal organ conveyance of charcoal at 100mg/kg weight expectantly transportation of thirty seven.21% (22.3333±7.05), extremely vital (P≤0.01 vs. saline group) each at 200mg/kg and 300mg/kg expectantly internal organ transportation of twenty five.91% (14.8000±2.16) and 20.89% (12.3333 ± 1.76383) severally (Tab. 3; Fig. 3).

Effect of Methanolic extract of leaf, fruit and stem bark of *Ehretia obtusifolia* on gastrointestinal motility

Leaf extract of *Ehretia obtusifolia* showed effectualness against diarrhea. The methanolic extract of leaf of experimented plant showed vital (P≤0.05 vs. saline group) result at 100mg/kg, and

extremely vital (P≤0.01 vs. saline group) at 200mg/kg and three hundred mg/kg dose level expectantly internal organ conveyance of charcoal thirty five.05%, 24.13% and 25.80% (20.3367 ± 2.02732, 14.000±0.00000, 15.2000±0.11547 mean values severally). *Ehretia obtusfolia* fruit showed extremely predominate (P≤0.01 vs. saline group) medicinal drug activity at 300mg/kg weight. At 100mg/kg and 200mg/kg it showed predominate (P≤0.05 vs. saline group) results compared to traditional saline (87%) and loperamide (14%). Fruit extract decrease transit of charcoal alimentation through minuscule bowel in purgative treated mice. Charcoal motility percentages in diminutive intestines were twenty.77%, 34.45%, 43.1% with mean values of twelve.4667±1.24544. 20.3333±1.76383 and twenty five.0333±2.88694, severally. Stem bark of *Ehretia obtusifolia* was in addition examine for medicinal drug efficiency and acquire extremely important results in the slightest degree dose levels e.g., 100mg/kg, 200mg/kg and 300mg/kg compared with management (87%) and normal drug (14%). Charcoal conveyance percentages were thirty two.27% with norm nineteen.3667±0.87623 at a hundred mg/kg (P≤0.05 vs. saline group), three result at 100mg/kg, and extremely vital (P≤0.01 vs. saline group) at 200mg/kg and three hundred mg/kg dose level expectantly internal organ conveyance of charcoal thirty five.05%, 24.13% and 25.80% (20.3367 ± 2.02732, 14.000 ± 0.000, 15.2000 ± 0.11547 mean values severally). *Ehretia obtusfolia* fruit showed extremely predominate (P≤0.01 vs. saline group) medicinal drug activity at 300mg/kg weight. At 100mg/kg and 200mg/kg it showed predominate (P≤0.05 vs. saline group) results compared to traditional saline (87%) and loperamide (14%). Fruit extract decrease transit of charcoal alimentation through minuscule bowel in purgative treated mice. Charcoal motility percentages in diminutive intestines were twenty.77%, 34.45%, 43.1% with mean values of twelve.4667 ± 1.24544, 20.3333±1.76383 and twenty five.0333±2.88694, respectively. Stem bark of *Ehretia obtusifolia* was in addition examine for medicinal drug efficiency and acquire extremely important results in the slightest degree dose levels e.g. 100mg/kg, 200mg/kg and 300mg/kg compared with management (87%) and normal drug (14%). Charcoal conveyance percentages were thirty two.27% with norm nineteen.3667±0.87623 at a hundred mg/kg (P≤0.05 vs. saline group), three result at 100mg/kg, and extremely vital (P≤0.01 vs. saline group) at 200mg/kg and three hundred mg/kg dose level expectantly internal organ conveyance of charcoal thirty five.05%, 24.13% and 25.80% (20.3367±2.02732, 14.000 ± 0.00000, 15.2000 ± 0.11547 mean values respectively). *Ehretia obtusfolia* fruit showed extremely predominate (P≤0.01 vs. saline group) medicinal drug activity at 300mg/kg weight. At 100mg/kg and 200mg/kg it showed predominate (P≤0.05 vs. saline group) results compared to traditional saline (87%) and loperamide (14%). Fruit extract decrease transit of charcoal alimentation through minuscule bowel in purgative treated mice. Charcoal motility percentages in diminutive intestines were twenty.77%, 34.45%, 43.1 % with mean values of twelve.4667±1.24544, 20.3333 ± 1.76383 and twenty five.0333 ± 2.88694, respectively. Stem bark of *Ehretia obtusifolia* was in addition examine for medicinal drug efficiency and acquire extremely important results in the slightest degree dose levels e.g. 100mg/kg, two hundred mg/kg and 300mg/kg compared with management (87%) and normal drug (14%). Charcoal conveyance percentages were thirty two.27% with norm nineteen.3667±0.87623 at a hundred mg/kg (P≤0.05 vs. saline group), 30.45% with norm seventeen.9667±1.03333 at two hundred mg/kg (P≤0.01 vs. saline group), and 27.00 you bored with norm sixteen.2000±2.61534 at 300mg/kg (P≤0.01vs. saline group) (Tab. 4; Fig. 3).

Effect of Methanolic extract of leaf, fruit and stem bark of *Ehretia obtusifolia* on gastrointestinal motility

Leaf extract of *Ehretia obtusifolia* showed effectualness against diarrhea. The methanolic extract of leaf of experimented plant showed vital (P≤0.05 vs. saline group) result at 100mg/kg, and extremely vital (P≤0.01 vs. saline group) at 200mg/kg and three hundred mg/kg dose level expectantly internal organ conveyance of charcoal thirty five.05%, 24.13% and 25.80% (20.3367 ± 2.02732, 14.000±0.00000, 15.2000±0.11547 mean values severally). *Ehretia obtusfolia* fruit showed extremely predominate (P≤0.01 vs. saline group) medicinal drug activity at 300mg/kg weight. At 100mg/kg and 200mg/kg it showed predominate (P≤0.05 vs. saline group) results compared to traditional saline (87%) and loperamide (14%). Fruit extract decrease transit of charcoal alimentation through minuscule bowel in purgative treated mice. Charcoal motility percentages in diminutive intestines were twenty.77%, 34.45%, 43.1% with mean values of twelve.4667±1.24544. 20.3333±1.76383 and

twenty five.0333±2.88694, severally. Stem bark of *Ehretia obtusifolia* was in addition examine for medicinal drug efficiency and acquire extremely important results in the slightest degree dose levels e.g., 100mg/kg, 200mg/kg and 300mg/kg compared with management (87%) and normal drug (14%). Charcoal conveyance percentages were thirty two.27% with norm nineteen.3667±0.87623 at a hundred mg/kg (P≤0.05 vs. saline group), three result at 100mg/kg, and extremely vital (P≤0.01 vs. saline group) at 200mg/kg and three hundred mg/kg dose level expectantly internal organ conveyance of charcoal thirty five.05%, 24.13% and 25.80% (20.3367 ± 2.02732, 14.000 ± 0.000, 15.2000 ± 0.11547 mean values severally). *Ehretia obtusfolia* fruit showed extremely predominate (P≤0.01 vs. saline group) medicinal drug activity at 300mg/kg weight. At 100mg/kg and 200mg/kg it showed predominate (P≤0.05 vs. saline group) results compared to traditional saline (87%) and loperamide (14%). Fruit extract decrease transit of charcoal alimentation through minuscule bowel in purgative treated mice. Charcoal motility percentages in diminutive intestines were twenty.77%, 34.45%, 43.1% with mean values of twelve.4667 ± 1.24544, 20.3333±1.76383 and twenty five.0333±2.88694, respectively. Stem bark of *Ehretia obtusifolia* was in addition examine for medicinal drug efficiency and acquire extremely important results in the slightest degree dose levels e.g. 100mg/kg, 200mg/kg and 300mg/kg compared with management (87%) and normal drug (14%). Charcoal conveyance percentages were thirty two.27% with norm nineteen.3667±0.87623 at a hundred mg/kg (P≤0.05 vs. saline group), three result at 100mg/kg, and extremely vital (P≤0.01 vs. saline group) at 200mg/kg and three hundred mg/kg dose level expectantly internal organ conveyance of charcoal thirty five.05%, 24.13% and 25.80% (20.3367±2.02732, 14.000 ± 0.00000, 15.2000 ± 0.11547 mean values respectively). *Ehretia obtusfolia* fruit showed extremely predominate (P≤0.01 vs. saline group) medicinal drug activity at 300mg/kg weight. At 100mg/kg and 200mg/kg it showed predominate (P≤0.05 vs. saline group) results compared to traditional saline (87%) and loperamide (14%). Fruit extract decrease transit of charcoal alimentation through minuscule bowel in purgative treated mice. Charcoal motility percentages in diminutive intestines were twenty.77%, 34.45%, 43.1 % with mean values of twelve.4667±1.24544, 20.3333 ± 1.76383 and twenty five.0333 ± 2.88694, respectively. Stem bark of *Ehretia obtusifolia* was in addition examine for medicinal drug efficiency and acquire extremely important results in the slightest degree dose levels e.g. 100mg/kg, two hundred mg/kg and 300mg/kg compared with management (87%) and normal drug (14%). Charcoal conveyance percentages were thirty two.27% with norm nineteen.3667±0.87623 at a hundred mg/kg (P≤0.05 vs. saline group), 30.45% with norm seventeen.9667±1.03333 at two hundred mg/kg (P≤0.01 vs. saline group), and 27.00 you bored with norm sixteen.2000±2.61534 at 300mg/kg (P≤0.01vs. saline group) (Tab. 4; Fig. 3).

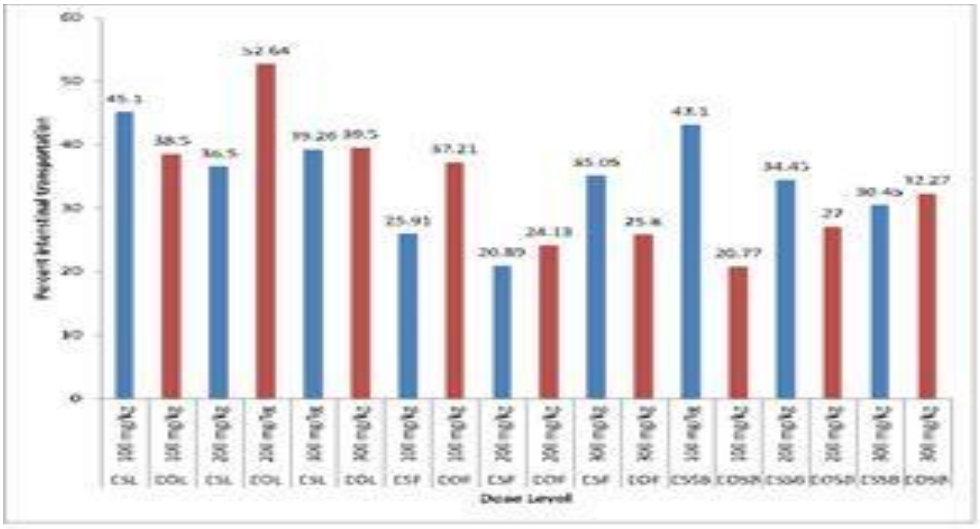

FIGURE 3 - Comparison of % intestinal transportation of *E. serrata* and *E. obtusifolia*

Table 2: Effect of the methanolic leaf, fruit and stem extracts of Ehretia obtusifolia on castor oil induced gastrointestinal transit in mice

	Dose (mg/kg)	Onset of diarrhea (Min)	No of wet faeces	Total No of faeces	Average weight of wet faeces (gm)	Average weight of total faeces (gm)	% inhibition of defecation	% WWFO	% WTFO
Control		69.33 ± 8.98	6.99 ±1.34	7.78 ±1.28	0.38 ± 0.06	0.40 ±0.05			
Loperamide		150.83 ±24. 34**	1.50 ± 0.70**	2.33 ± 0.92**	0.08 ± 0.05**	0.10 ± 0.06**	78.50	21.05	25.00
Leaves	100	78.13 ± 11.78	3.50 ± 0.68	4.33 ± 0.67*	0.27 ± 0.01	0.30 ± 0.01	49.92	71.05	75.00
	200	100.67 ± 12.67*	3.11± 0.91*	4.36 ± 0.81*	0.16 ± 0.04	0.19 ± 0.05*	55.50	42.10	47.50
	300	110.00 ± 13.45**	2.11 ± 0.63**	3.78 ± 0.51**	0.10 ± 0.01**	0.11 ± 0.04**	69.81	26.31	27.50
Fruits	100	102.33 ± 23.81*	3.50 ± 1.00	4.81± 1.34	0.20 ± 0.01*	0.21 ± 0.07*	45.63	52.63	52.50
	200	115.50 ± 19.99**	3.17 ± 0.81*	3.99± 0.80*	0.16 ± 0.06**	0.16 ± 0.09*	54.64	42.10	40.00
	300	130.62 ± 20.67**	2.18 ± 1.23**	3.45 ± 0.16**	0.12 ± 0.05**	0.13± 0.13**	68.81	31.57	32.50
Stem bark	100	102.22 ± 9.14*	5.00 ± 0.45	5.67 ± 0.36	0.28 ± 0.06	0.29 ± 0.08	28.46	73.68	72.50
	200	125.00 ± 22.02**	3.27 ± 0.81*	4.09 ± 1.05	0.22 ± 0.08*	0.23 ± 0.57*	53.64	57.89	57.50
	300	135.50 ± 29.86**	2.09 ± 0.95**	3.11 ± 1.31**	0.14 ± 0.05**	0.12 ± 0.19**	70.01	36.84	30.00

The data of castor oil induced gastrointestinal transit in mice of *Ehretia obtusifolia* are reported as mean ± SEM (n=5) and were analyzed through ANOVA following Dunnett's post-hoc, compared to control values, significant at *p≤0.05 and highly and highly significant at **p≤0.01.

Table 3: Effect of methanol extract of *Ehretia serrata* on distance travelled by charcoal in mice intestine, percentage intestinal transportation of charcoal and percentage of anti-diarrheal effect of methanol extracts after castor-oil induction diarrhea

S. No	Treatment	Dose (mg/kg)	Distance travelled by charcoal	% intestinal transportation	% anti-diarrhoeal effect	% inhibition
1	Normal saline		51.333±9.222	87.00	13	
2	Loperamide	3	8.3333±0.66	14	86	83.77
3	Leaf	100	26.000±0.57	45.1	54.9	49.31
		200	22.3367±0.33*	38.5	61.5	54.59
		300	20.7667±0.23*	36.5	63.5	59.55
4	Fruit	100	30.0300±2.50	52.64	47.36	41.49
		200	22.7333±5.62*	39.26	60.74	55.71
		300	23.7000±4.97*	39.5	60.5	53.82
5	Stem bark	100	22.3333±7.05*	37.21	62.79	56.49
		200	14.8000±2.16**	25.91	74.00	71.16
		300	12.3333±1.76**	20.89	79.11	75.97

The data of the anti-diarrhoeal activity of *Ehretia serrata* are reported as mean ± SEM and were analyzed through ANOVA following Dunnett's post-hoc, significant at *p≤0.05 and highly significant at **p≤0.01.

Table 4: Effect of methanol extract of *Ehretia obtusifolia* on distance travelled by charcoal in mice intestine, percentage intestinal transportation of charcoal and percentage of anti-diarrheal effect of methanol extracts after castor-oil induction diarrhea

S. No		Dose (mg/kg)	Distance travelled by charcoal	% intestinal transportation	% anti-diarrhoeal effect	% inhibition
1	Normal saline	-	51.333±9.222	87.00	13	-
2	Loperamide	3	8.3333±0.66667	14	86	83.71
3	Leaf	100	20.3367±2.02732*	35.05	64.95	60.39
		200	14.000±0.00000**	24.13	75.87	72.72
		300	15.2000±0.11547**	25.80	74.2	70.38
4	Fruit	100	25.0333±2.88694*	43.1	56.9	51.28
		200	20.3333±1.76383*	34.45	65.55	60.39
		300	12.4667±1.24544**	20.77	79.23	75.71
5	Stem bark	100	19.3667±0.876238*	32.27	67.73	62.27
		200	17.9667±1.03333**	30.45	69.55	64.99
		300	16.2000±2.61534**	27.00	73.00	68.43

Table 5: *In vivo* anti-diarrheal index value of the methanolic extract of leaf, fruit and stem bark extract of *Ehretia serrate*

S. No	Drug treatment	Dose (mg/kg)	Delay in defecation time (Dfreq)	Gut meal travel reduction (Gmeq)	Purging frequency (Pfreq)	Antidiarrheal index ADI
1	Normal saline	-				
2	Loperamide	3	127.30	70.98	83.76	91.13
3	Leaf	100	72.71	54.61	49.31	58.06
		200	88.41	62.62	54.59	67.19
		300	125.11	68.30	59.55	79.83
4	Fruit	100	52.92	35.33	41.49	42.64
		200	76.32	48.13	55.71	58.92
		300	99.87	59.48	53.82	68.37
5	Stem bark	100	40.45	35.17	56.49	43.15
		200	59.13	49.59	71.16	59.31
		300	110.69	65.80	75.97	82.09

In vivo antidiarrheal index value of *Ehretia obtusifolia*

The *in vivo* medicinal drug index (ADI) was measured by considering Dfreq (delay in onset of defecation), Gmeq (Distance lined by meal in gut) and Pfreq (purging frequency) as major parameters. most ADI were showed at 300mg/kg doses of leaf (66.05), fruit (77.22) and stem bark (77.07) methanolic extracts. At dose 200mg/kg the very best ADI worth (65.41) was showed by stem bark methanolic extract. Least ADI was thirty four.00 showed by leaf extract at dose level 100mg/kg (Tab. 6).

Phytochemical screening leaf, fruit and stem bark of *Ehretia serrata*

Phytochemical screening of the methanolic leaf, fruit and stem bark extract of *Ehretia serrata* disclosed that the presence of phenol compounds, starch, protein, reducing sugar, steroids, tarpenoids, Aldehydes, glycosides, amino acids, saponine, alkaloids, as major constituents except fix oil, and phlobatannin that were absent in stem bark and gift in different 2 elements and tannins that was absent in fruit and gift in leaf and stem bark (Tab. 7).

Phytochemical screening of leaf, fruit and stem bark of *Ehretia obtusifolia*

The preliminary phytochemical screening of the methanolic extract of *Ehretia obtusifolia* leaf, fruit and stem bark disclosed the presence of phenol compounds, flavonoids, starch, protein, reducing sugar, steroids, tarpenoids, fats, glycosides, amino acids, saponine, and alkaloids altogether elements. organic compound and anthraquinone weren't detected altogether elements. oil and phlobatannin were absent solely in stem bark and tannic acid in fruit of *Ehretia obtusifolia* (Tab. 8).

Table 6: *In vivo* anti-diarrheal index value of the methanolic extract of leaf, fruit and stem bark extract of *Ehretia obtusifolia*

S. No	Drug treatment	Dose (mg/kg)	Delay in Defecation time (Dfreq)	Gut meal travel reduction (Gmeq)	Purging frequency (Pfreq)	Antidiarrheal index ADI
1	Normal saline	-				
2	Drug treatment	3	117.55	78.50	83.76	91.77
3	Leaf	100	13.04	49.92	60.39	34.00
		200	45.20	55.50	72.72	56.71
		300	58.66	69.81	70.38	66.05
4	Fruit	100	47.59	45.63	51.28	48.11
		200	66.59	54.64	60.39	60.34
		300	88.40	68.81	75.71	77.22
5	Stem bark	100	47.43	28.46	62.27	43.80
		200	80.29	53.64	64.99	65.41
		300	95.44	70.01	68.43	77.03

Table 7: List of Phyto-constituents found in leaf, fruit and stem bark of *Ehretia serrate*

S. No	Name of functional group	Leaves	Fruit	Stem bark
1	Phenol compounds	+	+	+
2	Starch	+	+	+
3	Protein	+	+	+
4	Reducing sugar	Light green	Red	Reddish brown
5	Steroids	+	+	+
6	Terpenoids	+	+	+
7	Fixed oil	+	+	-
8	Aldehydes	-	-	-
9	Anthraquinone	-	-	-
10	Glycosides	+	+	+
11	Amino acids	+	+	+
12	Saponine	+	+	+
13	Alkaloids	+	+	+
14	Tannins	+	-	+
15	Phlobatannin	+	+	-

Table 8: List of Phyto-constituents in leaf, fruit and stem bark of *Ehretia obtusifolia*

S. No	Name of functional Group	Leaves	Fruit	Stem bark
1	Phenol compounds	+	+	+
2	Starch	+	+	+
3	Protein	+	+	+
4	Reducing sugar	Greenish brown	Red	Greenish orang
5	Steroids	+	+	+
6	Terpenoids	+	+	+
7	Fixed oil	+	+	-
8	Aldehydes	-	-	-
9	Anthraquinone	-	-	-
10	Glycosides	+	+	+
11	Amino acids	+	+	+
12	Saponine	+	+	+
13	Alkaloids	+	-	+
14	Tannins	+	+	+
15	Phlobatannin	+	-	+

DISCUSSION

The present work was marked to judge the medicinal drug activity of the methanolic extract of leaf, fruit and stem bark extract of *Ehretia serrata* and *Ehretia obtusifolia* by victimization 2 experimental styles of looseness of the bowels in mice. In each models, looseness of the bowels was made in mice by giving purgative to every mice. Unsaturated fatty acid is an energetic substance found in purgative that it turns out by action of enzyme accelerator in higher internal organ half, cause looseness of the bowels (Kulkami and Pandit, 2005). It works by binding with EP3 prostanoid receptors on sleek muscle cells of bowel and prevents absorption and enhances fluids and solution accumulation by secretion (Tunaru et al. 2012; Racusen and Binder, 1979). This substance additionally disturbed the epithelial duct motility action of sleek muscles (Matias et al. 1978). Within the 1st model "castor oil elicited looseness of the bowels model" the extract showed extremely vital impact on all measured parameters: onset of looseness of the bowels, the quantity of wet and total stools and weight of wet stools. This results in agreement with the report on the methanolic leaf, fruit and stem bark extract of *Ehretia serrata* and *Ehretia obtusifolia* (Bakare et al. 2011; Mengistu et al. 2015). Previous study advised that each one anti-diarrheal medication showed medicinal drug impact by inhibition of autacoid formation. Gift medicinal drug impact of varied extract is also related to the inhibition of autacoid synthesis (Gidwani et al. 2009). This correlation is evidenced by the prompt of prostaglandins formation once purgative induction in gut (Robert et al. 1976; Taufiq-Ur-Rahman et al. 2005). The phytochemical screening of the extracts showed the presence of varied vital bioactive compounds, that valid the inhibitions of prosglandin production like flavonoids and phytosterol. These 2 compounds altered the assembly of Cox one and a pair of and lipooxygenase production; thus, inhibit autacoid production (Awad et al. 2004; Hamalainen et al. 2011). Tannins additionally play vital role in anti-diarrheal impact. Tannic acid with protein forms tannate that showed resistance to the chemical alteration in bowel; thence scale back internal organ secretion and peristaltic movement (Ashok and Upadhyay, 2012). Presence of these bioactive compounds in numerous elements extracts of *Ehretia serrata* and *Ehretia obtusifolia* evidenced the impact of those bioactive constituents within the anti-diarrheal activity. Medicinal drug agents largely decreasing secretion and deceleration the GI sleek muscles propulsive movements. Therefore, to urge a lot of data regarding mechanism, extract was additional investigated by evaluating little internal organ motility tests. Within the little internal organ transit take a look at, the charcoal meal methodology was designated. The extracts were considerably reducing GI motility or transit, the impact were dose dependent and better doses

(300mg/kg) altogether elements extract showed higher restrictive effects. The decrease of GI motility is one mechanism by that several medicinal drug agents will act (Ezekwesili et al. 2010; Qnais et al. 2007). The results were ascertained by induction of extracts once purgative induce looseness of the bowels.All elements extract of each experimented plants considerably ($p>0.01$) reduced internal organ transit by perceptive the decrease in GI motility of the charcoal meal. These results counsel the effectiveness of extracts of each plants on all elements of bowel and increase the keep of charcoal meal in bowel. Therefore, the absorption time of gear increase in bowel (Islam et al. 2013). Reduced internal organ propulsive movement of bowel of mice is also related with the anti-motility impact of leaf, fruit and stem bark extracts of each examined plants. The greatest impact of the all elements of extract were extremely like the impact showed by loperamide a very important drug use for looseness of the bowels elicited by purgative (Begum et al. 2013).

The aperient contains unsaturated fatty acid, a vital bioactive constituent that manufacture inflammation and irritation in enteric tissue layer, resulting in unharness of prostaglandins. The prostaglandins inhibit the NaCl and water organic process (Pierce et al. 1971). Tannins decrease fluid secretion by inhibiting CFTR and CaCC, by generating a protein-precipitating reaction to the GI membrane (Ashok and Upadhyay, 2012; Wongsamitkul et al. 2010). Those medications are more practical in diarrhoeic condition that inhibits enteric transit (Silva et al. 2012). Results discovered that every-one doses of all components were effective in inhibition of GI transit as compared with the management. Presence of flavonoids (Di Carlo et al., 1993) and tannins (Ashok and Upadhyay, 2012) in most components of each plants extracts are analyzed to possess medicament activity thanks to their ability of decreasing enteric substances transit. This inhibition of GI transit could also be the mix result of flavonoids and tannic acid. This can be the action of those bioactive compounds to prolong the time of drugs in bowel and delayed the peristaltic movement of bowel. In vivo, anti-diarrhoeic index is that the combined could be a live of the collective effects of the various parts of diarrhoea, like the onset of diarrhoeic stools, purging frequency, and enteric movement frequency (Than et al., 1989). This parameter showed the effectiveness of extracts against diarrhoea. The ADI price is that the dose dependent parameter. the best elite dose of the extract, with the best ADI value, is endued with the simplest medicament activity.

CONCLUSION

Present study on *Ehretia serrata* and *Ehretia obtusifolia* conform the presence of therapeutically important phytoconstituents, their safe usage and to rationalize its traditional uses as anti- diarrheal agent. This study will also be helpful to commercialize these plants in the production of cheap plant based pharmaceutical preparations in third world countries. Further explorative work is required to isolate the active constituents, their mechanistic approach and commercialization.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

Zill-E-Huma performed the experiment. Mohammad Ibrar and Barkatullah designed and supervised the experiment, Ishfaq Hameed and Memrez Khushal Gigyani wrote the manuscript. All authors read and approve the manuscript.

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