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Phramacotherapeutic Evaluation of *Parmentiera cereifera* Seem. (Family Bignoniaceae) Cultivated in Egypt on Albino Rats

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Authors' contributions

This work was carried out in collaboration between all authors. All authors designed the study and wrote the protocol. Author NMAW wrote the first draft of the manuscript. Authors NMAW, ANESH and HEK managed the literature searches. Author NMAW managed the analyses of the study. Authors MSK, NMAW and ANESH revised the written manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Aims: The current study evaluates different biological activities viz., anti-inflammatory, anti-hyperglycemic and gastroprotective of methanolic extracts (MEs) of different parts viz., [mixture of leaves & stems (1:3) (MLS13), flowers and stem barks] and different fractions of ME of MLS13 of *Parmentiera cereifera* Seem. Moreover, this study estimates LD_{50} of ME of MLS13.
Place and Duration of Study: The study was carried out for nine months in 2012 in the Department of Pharmacology, Faculty of Medicine and Department of Pharmacognosy and Phytochemistry, Faculty of Pharmacy, Minia University, Minia, Egypt.
Methodology: The different MEs of various parts such as MLS13, flowers and stem barks and the

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different fractions of ME of MLS13 of *P. cereifera* were used in the present study. The different pharmacological activities such as anti-inflammatory, anti-hyperglycemic, gastroprotective and LD_{50} were determined using animal models as described in standard methods.

Results: In yeast-induced paw edema method, ME of MLS13 had the highest anti-inflammatory activity (****P<0.001*). While, in carrageenan-induced paw edema method, the highest anti-inflammatory activity (****P<0.001*) was exhibited by ME of stem barks. Moreover, both ME of flowers (****P<0.001*) and ethyl acetate (EtOAc) fraction (****P<0.01*) exhibited significant anti-hyperglycemic activity in alloxan-induced diabetes method. Furthermore, in indomethacin-induced gastric ulcer method, the highest gastroprotective effect (****P<0.001*) was demonstrated by the petroleum ether (pet. ether) fraction. Finally, there is no toxicity symptoms of ME of MLS13 of *P. cereifera* up to 5 gm/kg.

Conclusion: The biological results revealed that *P. cereifera* may be used in the development of various pharmaceutical preparations viz., anti-infalammatory, anti-hypergycemic as well as gastroprotective drugs, due to its wide safety margin.

Keywords: Parmentiera cereifera seem; Bignoniaceae; albino rats; leaves & stems; stem bark; flower; anti-inflammatory; anti-hyperglycemic; gastroprotective.

1. INTRODUCTION

Family Bignoniaceae includes many genera and species with various therapeutic uses. Anti-inflammatory activity was displayed by many species viz., *Pyrostegia venusta* [1]*, Arrabidaea brachypoda* [2]*, Tecoma stans* [3]*, Kigelia pinnata* [4] and *K. africana* [5]. While, many plants as *Newbouldia laevis* [6], *K. pinnata* [7]*, Oroxylum indicum* [8] *and Parmentiera edulis* [9, 10] demonstrated different degrees of anti-diabetic activity. Moreover, gastroprotective effect was shown by *O. indicum*in [11] and *Spathodea campanulata* [12]. One of the above mentioned family is *Parmentiera cereifera* Seem. It is known as Candle tree, Candlestick tree and Panama Candle tree [13]. The leaf ME of *P. cereifera* was studied for its phenols and polyphenols content [14]. While, another study dealt with the isolation of seven compounds viz., phenolic acid glycosides (parmentins A and B), two steroid compounds [(β-sitosterol & stigmasterol mixture) and β-sitosterol glucoside) and three phenolic acids (vanillic, isovanillic and p-hydroxybenzoic) from ME of the mixture of leaves & stems of the same plant [15]. A thorough survey of literature indicated that this plant was not extensively studied pharmacologically and phytochemically. From the preceding, we were inspired to find anti-inflammatory, anti-hyperglycemic and gastroprotective activities of *P. cereifera* on albino rats. Moreover, the current study estimates LD_{50} of ME of MLS13 of the plant.

2. MATERIALS AND METHODS

2.1 Materials

2.1.1 Plant material and preparation of extracts and fractions

The plant was cultivated in El-Zohria botanical garden, Giza, Egypt. The MLS13 were collected in February 2009. The flowers and stem barks were collected in October 2011. The plant was kindly identified by Dr./Mamdouh Shokry, General Manager of El-Zohria garden. It was kept in the Herbarium of Pharmacognosy Department, Faculty of Pharmacy, Minia University, Minia, Egypt with voucher specimen number (Mn-Ph-Cog-003).

The air-dried fine powdered (MLS13, 5 kg), (flowers 20 gm) and (stem barks 30 gm) of *P. cereifera* were each separately extracted by maceration with absolute methanol till exhaustion and then concentrated under reduced pressure by using rotary evaporator till dryness to yield 156, 5 and 2 gm, respectively. The concentrated ME of MLS13 was suspended in the least amount of distilled water, transferred to a separating funnel and partitioned successively with pet. ether, $CHCl_3$ and EtOAc. The obtained fractions were concentrated by using rotary evaporator under reduced pressure to afford 3 fractions: pet. ether (20 gm), $CHCl_3$ (4 gm) and EtOAc (10 gm). The residual aqueous mother liquor was also concentrated by the same method to yield the fourth aqueous fraction (120 gm).

2.1.2 Animals

The animals used in the present study included male albino rats weighing about (90-100) and (200-220) gm. The animals were housed under standardized environmental conditions, fed with standard diet, water and left to acclimatize to the environment for one week prior to inclusion in the experiments. The animals were handled only at the time of experiments and during cages cleaning. All conditions were made to diminish animal suffering. Procedures relating animals and their care were conducted in conformity with the institutional guidelines of Minia University, Minia, Egypt and it conforms to the provisions of the Declaration of Helsinki in 1995.

2.1.3 Statistical analysis

The results are expressed in terms of means ± S.E.M. Statistically significant difference was determined using one-way analysis of variance (ANOVA) followed by Dunnett's test. Probability values of (**P<0.05, **P<0.01,*** P<0.001*) indicated statistical significance.

2.2 Techniques

2.2.1 Determination of the median lethal dose (LD_{50}) of ME of MLS13 of *P. cereifera*

The LD_{50} of ME of MLS13 of *P. cereifera* was determined by suspending the dried ME in 0.5% carboxymethylcellulose (CMC) in distilled water and was administered orally to four-week-old male albino rats [16] in graded doses up to 5 gm/kg body weight. Male albino rats (200-220 gm) were used in the experiment. The rats were randomly divided into 2 groups (4 rats per group). The control group received the same volumes of vehicle of ME. The animals were observed for any signs of toxicity and mortality for the first critical 4 hrs and till the end of 24 hrs [17]. Signs of toxicity to be observed include paw-licking, stretching, respiratory distress, diarrhea and death [18].

2.2.2 Anti-inflammatory activity

The anti-inflammatory activity was evaluated using two different methods for induction of inflammation [19].

2.2.2.1 Determination of anti-inflammatory activity of MEs of different parts of P. cereifera using yeast-induced paw edema method

The MEs of different parts viz., MLS13, flowers and stem barks of *P. cereifera* were tested for their anti-inflammatory activity using yeast-induced paw edema method [19]. Male albino rats (200-220 gm) were used in the experiment. They were randomly divided into 5 groups (4 rats per group). The different MEs were suspended in CMC (0.5% solution in distilled water) and administered orally to the rats at a dose of 300 mg/kg body weight. The control group received an equal volume of vehicle of plant MEs orally. While, the reference drug indomethacin 8 mg/kg per oral (po) was given to another group [20]. Inflammation was induced by subcutaneous injection of 10 ml/kg 20% yeast suspension in normal saline into the sub-plantar tissue of the right hind paw of each rat, 24 hrs prior to administration of the tested MEs and the reference drug [21]. Paw thickness (mm) was measured by a vernier caliper [22] immediately (0 hr) and 1, 2, 3 and 4 hrs after administration of the tested MEs and reference drug.

The groups were specified as follows:

Group 1: Control.
Group 2: ME of MLS13.
Group 3: ME of flowers.
Group 4: ME of stem barks.
Group 5: Indomethacin.

2.2.2.2 Determination of anti-inflammatory activity of MEs of different parts of P. cereifera using carrageenan-induced paw edema method

The anti-inflammatory activity of MEs was evaluated using carrageenan-induced paw edema method [21]. The experiment was carried out on male albino rats (200 gm). The rats were randomly divided into 5 groups (4 rats per group). The phlogistic agent employed in this study was 0.1 ml carrageenan suspension (1% w/v in normal saline solution) injected subcutaneously into the sub-plantar area of the right hind paw [21]. The MEs were diluted in CMC (0.5% solution in distilled water) and administered orally to rats at a dose of 300 mg/kg body weight one hr prior to injection of carrageenan. The control group received an equal volume of CMC orally (vehicle of plant MEs), while the reference drug (indomethacin 8

mg/kg) was given to another group [20]. Paw thickness (mm) was measured by a vernier caliper [22] immediately (0 hr) and 1, 2, 3 and 4 hrs after administration of carrageenan.

The groups were specified as follows:

Group 1: Control.
Group 2: ME of MLS13.
Group 3: ME of flowers.
Group 4: ME of stem barks.
Group 5: Indomethacin.

2.2.3 Evaluation of anti-hyperglycemic activity of different MEs and fractions of *P. cereifera* using alloxan-induced diabetes method

The anti-hyperglycemic activity of MEs of different parts: MLS13, flowers and stem barks of *P. cereifera*, in addition to the different fractions as in section (2.1.1), which were obtained from fractionation procedure of ME of MLS13 of the investigated plant were tested on alloxan-induced diabetic rats. A freshly prepared solution of alloxan monohydrate dissolved in the sterile normal saline at a dose of 150 mg/kg body weight was injected intraperitoneal (ip) to male albino rats (200-220 gm) [23]. The development of hyperglycemia was verified 3 days after alloxan injection [24]. Rats with fasting blood glucose levels (BGLs) above 130 mg/dl were considered to be diabetic rats and were used in this study [25,26]. Diabetic rats were divided into 9 groups (4 rats per group). The tested MEs and fractions of *P. cereifera* were diluted in CMC (0.5% solution in distilled water) and administered (ip) to rats at a dose of 300 mg/kg [9]. The control group received the vehicle of plant MEs (0.5% CMC solution, ip), while the reference drug (glibenclamide 0.5 mg/kg) was administered (po) to another group [27,28]. BGLs were measured at intervals of 0 (fasting), 1, 2, 3 and 4 hrs by AccuCheck® Active Roche (Model GC, Mannheim, Germany). The blood samples were taken from the tail vein. The percentage of change in BGL was calculated according to the following equation [29].

$$\% \text{ Glycemic change} = \frac{\text{Glucose level after time (hr)} - \text{Fasting blood glucose}}{\text{Fasting blood glucose}} \text{X100}$$

The groups were specified as follows:

Group 1: Control (0.5% CMC solution).
Group 2: ME of MLS13.
Group 3: Pet. ether fraction of MLS13.
Group 4: $CHCl_3$ fraction of MLS13.
Group 5: EtOAc fraction of MLS13.
Group 6: Aqueous fraction of MLS13.
Group 7: ME of flowers.
Group 8: ME of stem barks.
Group 9: Glibenclamide.

2.2.4 Determination of the gastroprotective activity of different MEs and fractions of *P. cereifera* using indomethacin-induced gastric ulceration method

Albino rats (90-100 gm) were fed with a standard diet of commercial rat chow and tap water and left to acclimatize to the environment for one week prior to inclusion in the experiments. Rats were fasted for 24 hrs prior to the experiment in mesh-bottomed cages to minimize coprophagia with free access to water [30]. Indomethacin-induced gastric ulceration model is employed in this experiment. The different MEs and fractions of *P. cereifera* as in (section 2.1.1) were suspended in CMC (0.5% solution in distilled water) and administered orally to rats at a dose of 300 mg/kg body weight one hr prior to the administration of indomethacin. Gastric ulceration was induced by a large dose of indomethacin (40 mg/kg) administered orally [31]. Ranitidine was administered at a dose of (50 mg/kg) orally as a reference drug [32]. The rats were randomly divided into 9 following groups (4 rats per group):

Group 1: Control (in which rats received no further medication other than indomethacin).
Group 2: ME of MLS13.
Group 3: Pet. ether fraction of MLS13.
Group 4: $CHCl_3$ fraction of MLS13.
Group 5: EtOAc fraction of MLS13.
Group 6: Aqueous fraction of MLS13.
Group 7: ME of flowers.
Group 8: ME of stem barks.
Group 9: Ranitidine.

The rats were sacrificed by cervical dislocation 5 hrs after indomethacin administration. Their stomachs were removed and opened along the greater curvature. Then, they were washed with ice-cold saline and scored for macroscopic gross mucosal lesions. The lesions of gastric mucosa were expressed in terms of ulcer index (U.I.), which depends on calculating the ulcers by using a 0-3 scoring system based on the severity of these lesions [33]. The results are recorded in (Table 5). After recording the ulcers produced, the stomachs were fixed in 10% formalin

solution. After 24 hrs of fixation, embedding in a paraffin block, the stomachs were cut into sections of 5 µm onto a glass slide and stained with hematoxylin-eosin dye (HED) for histological assessment of the gastric mucosa as shown in (Fig. 1).

2.2.4.1 Assessment of gastric mucosal lesions

Gastric mucosal lesions in each stomach were measured and the ulcer score for each stomach was expressed as the total length of gastric lesions in that stomach. Afterwards, the mean ulcer score for each group was calculated.

The preventive index (P.I.) of different MEs and fractions of the plant was calculated from the following equation [34].

$$\%\ \mathrm{P.I.} = \frac{(\mathrm{U.I.\ of\ ulcered\ group}) - (\mathrm{U.I.\ of\ treated\ group})}{(\mathrm{U.I.\ of\ ulcered\ group})} \mathrm{X}100$$

3. RESULTS

3.1 LD_{50} Determination

It revealed that ME of MLS13 of *P. cereifera* didn't induce toxic symptoms or death up to 5 gm/kg.

3.2 Anti-inflammatory Activity

3.2.1 Determination of anti-inflammatory activity of MEs of different parts of *P. cereifera* using yeast-induced paw edema method

The results are summarized in (Table 1).

3.2.2 Determination of anti-inflammatory activity of MEs of different parts of *P. cereifera* using carrageenan-induced paw edema method

The results are recorded in (Table 2).

3.3 Evaluation of Anti-hyperglycemic Activity of MEs and Fractions of *P. cereifera* Using Alloxan-induced Diabetes Method

The results are listed in (Tables 3 and 4).

3.4 Gastroprotective Activity

3.4.1 Determination of gastroprotective activity of MEs and fractions of *P. cereifera* using indomethacin-induced gastric ulceration method

The results are summarized in (Table 5) and the histopathological study is illustrated in (Fig.1).

3.4.2 Histopathological results

(Fig. 1) shows the different pathological effects of control, pet. ether and ranitidine groups. The effects were described as follows:

Group 1: Control (Indomethacin):

The HED pictures show complete ulceration of the mucosa with haemorrhage and congestion of blood vessels. Inflammatory cells are found infiltrating the mucosa and sub-mucosa as shown in (Figs. 1A and 1B).

Group 3: Pet. ether fraction-pretreated group:

The HED picture shows partial shedding of the mucosa that indicates certain degree of gastroprotection exerted by pet. ether fraction. Inflammatory cells are found as well as infiltrating the mucosa and sub-mucosa as shown in (Fig. 1C).

Group 9: Ranitidine-pretreated group:

The HED picture shows partial shedding of the mucosa and inflammatory cells infiltration was also shown in (Fig. 1D).

4. DISCUSSION

4.1 LD_{50} Determination

Due to the great difference between the therapeutic dose 300 mg/kg and this dose 5 gm/kg without any sign of toxicity, this indicates a wide safety margin for the investigated ME of MLS13.

4.2 Anti-inflammatory Activity

4.2.1 Determination of anti-inflammatory activity of MEs of different parts of *P. cereifera* using yeast-induced paw edema method

The results in (Table 1) showed that ME of stem barks exhibited strong anti-inflammatory activity (***P<0.01*) after 2 hrs, which was like

indomethacin. After 3 hrs, both MEs of flower and stem barks exhibited strong anti-inflammatory activity (**P<0.05*) compared to the reference drug. The highest anti-inflammatory activity was displayed by ME of MLS13 (****P<0.001*) after 4 hrs of administration. While, ME of stem barks was the least active extract (**P<0.05*) after 4 hrs against yeast-induced paw edema. The anti-inflammatory activity may be attributed to the presence of sterols and glycosides [35]. This reduction may be related to the presence of β-sitosterol, stigmasterol, β-sitosterol glucoside, which were isolated from this species [15] and possess potent anti-inflammatory activity [36].

4.2.2 Determination of anti-inflammatory activity of MEs of different parts of *P. cereifera* using carrageenan-induced paw edema method

The results in (Table 2) revealed that all the tested extracts significantly decreased the paw edema induced by carrageenan. The highest anti-inflammatory activity after 3 and 4 hrs was exhibited by MEs of stem barks (****P<0.001*), followed by MLS13 (****P<0.001*) and finally flowers (****P<0.001*). The reduction of the anti-inflammatory activity could be explained as that of the previous method (yeast-induced paw edema model).

4.3 Evaluation of Anti-hyperglycemic Activity of MEs and Fractions of *P. cereifera* Using Alloxan-induced Diabetes Method

The results of anti-hyperglycemic activity of different MEs and fractions of *P. cereifera* on BGL in alloxan-induced diabetic rats were recorded in (Tables 3 and 4) showing that both flowers ME (****P<0.001*) and EtOAc fraction (***P<0.01*) exhibited significant anti-hyperglycemic activity after 4 hrs. The highest reduction of BGL percentage were (-60.80%) and (-34.80%) for flowers ME and EtOAc fraction, respectively. These reduction in BGL was comparable to the reference drug (glibenclamide). Many secondary metabolites were isolated from this plant e.g. phenolic acid glycosides, sterols, steroidal glycoside and phenolic acids [15]. The significant effect of EtOAc fraction may be attributed to its content of secondary metabolite e.g. 4-hydroxybenzoic acid [15,37]. Moreover, the significant reduction in BGL may be also attributed to the existence of certain phytoconstituents viz., sterols and polyphenolic compounds [38-41], where sterols have the capability of stimulating the pancreatic β-cells [38].

4.4 Gastroprotective Activity

4.4.1 Determination of gastroprotective activity of MEs and fractions of *P. cereifera* using indomethacin-induced gastric ulceration method

The results in (Table 5) revealed that different MEs and fraction of *P. cereifera* have a significant gastroprotective activity against indomethacin-induced ulceration model. The pet. ether fraction showed the highest gastroprotective activity (****P<0.001*), which was even higher than that of the reference drug ranitidine *(***P<0.001)*. The preventive index (93.00%) was obtained by pet. ether fraction, which was comparable to ranitidine (92.50%). The histopathological findings (Fig. 1) further confirmed these results. The highest gastroprotective effect of the pet. ether fraction among all the tested MEs and fractions may be attributed to the high content of sterols in this fraction [15,42]. β-Sitosterol and stigmasterol, which are the major component of the pet. ether fraction of ME of MLS13 are reported to illustrate effective gastric protection [15,42].

Table 1. Results of anti-inflammatory activity of MEs of different parts of *P. cereifera* using yeast-induced paw edema method

Group	Thickness of the paw (mm) after				
	0 hr	1 hr	2 hrs	3 hrs	4 hrs
Control	10.00±0.71	9.50±0.29	8.75±0.25	8.75±0.25	8.75±0.25
ME of MLS13	10.00±0.41	9.75±0.25	8.50±0.29	7.38±0.24*	6.89±0.13***
ME of flowers	10.25±0.25	9.00±0.00	8.50±0.29	7.63±0.24*	7.00±0.00***
ME of stem barks	11.00±0.00	9.00±0.00	7.25±0.14**	7.63±0.38*	8.00±0.00*
Indomethacin	10.75±0.25	9.25±0.25	7.25±0.14**	7.75±0.25	7.13±0.24***

*(*P<0.05, **P<0.01, *** P<0.001) compared to the control group. Data are presented as mean ± S.E.M in each group. (n = 4) rats in each group*

Table 2. Results of anti-inflammatory activity of MEs of different organs *P. cereifera* using carrageenan-induced paw edema method

Group	Thickness of the paw (mm) after				
	0 hr	1 hr	2 hrs	3 hrs	4 hrs
Control	6.00±0.00	5.00±0.00	6.00±0.00	6.00±0.00	6.00±0.00
ME of MLS13	6.13±0.13	5.75±0.25	4.75±0.25**	4.00±0.35***	3.88±0.43***
ME of flowers	6.38±0.13	5.25±0.25	4.38±0.24***	4.25±0.15***	4.00±0.20***
ME of stem barks	6.00±0.00	5.00±0.00	4.50±0.29***	3.50±0.00***	3.75±0.14***
Indomethacin	6.13±0.13	5.75±0.14	4.25±0.14***	4.75±0.14***	3.75±0.14***

*(*P<0.05, **P<0.01, *** P<0.001) compared to the control group. Data are presented as mean ± S.E.M in each group. (n = 4) rats in each group*

Table 3. Results of anti-hyperglycemic activity of different MEs and fractions of *P. cereifera* using alloxan-induced diabetes method

Group	Blood Glucose Level (BGL) (mg/dl)				
	0 hr	1 hrs	2 hrs	3 hrs	4 hrs
Control	142.8±3.8	142.3±3.9	143.0±4.4	143.0±4.4	142.0±4.4
ME of MLS13	180.7±6.0	267.7±16.5	259.0±16.2	169.7±9.0	135.0±8.7
Pet. ether fraction	163.7±3.8	133.7±1.5*	131.7±11.3**	142.7±3.8	126.7±2.6**
$CHCl_3$ fraction	143.7±0.3	139.7±13.6	123.7±4.3	124.7±8.4	126.7±9.5
EtOAc fraction	169.3±4.1	127.7±12.6*	111.7±11.3**	118.0±5.8*	110.3±11.9**
Aqueous fraction	401.7±6.6	437.3±63.4	416.0±86.2	254.7±17.3	201.3±8.9*
ME of flowers	332.0±0.6	240.0±0.6***	182.0±1.2***	333.0±0.6	130.0±1.2***
ME of stem barks	141.3±2.2	192.8±19.0	271.3±67.9	269.0±72.7	248.5±67.1
Glibenclamide	172.7±1.5	166.0±15.0	118.7±15.3	117.7±16.5*	101.7±12.4*

*(*P<0.05, **P<0.01, *** P<0.001) compared to 0 hr. Data are presented as mean ± S.E.M in each group. (n = 4) rats in each group*

Table 4. Effects of different MEs and fractions of *P. cereifera* on % change of BGL using alloxan-induced diabetes method

Group	% Glycemic change			
	1 hr	2 hrs	3 hrs	4 hrs
Control	-0.40	+0.10	+0.10	-0.60
ME of MLS13	+48.10	+43.30	-6.10	-25.30
Pet. ether fraction	-18.10	-19.40	-12.60	-22.60
$CHCl_3$ fraction	-2.80	-14.00	-13.20	-11.80
EtOAc fraction	-24.60	-34.00	-30.30	-34.80
Aqueous fraction	+8.90	+3.60	-36.60	-49.90
ME of flowers	-27.70	-45.20	+0.30	-60.80
ME of stem barks	+36.40	+92.00	+90.40	+75.90
Glibenclamide	-3.90	-31.30	-31.80	-41.10

Table 5. Results of gastroprotective activity of different MEs and fractions of *P. cereifera* using indomethacin-induced gastric ulceration method

Group	Ulcer index (U.I.)	Preventive index (P.I.) %
Control	40.00±0.65	-------
ME of MLS13	4.30±2.30***	89.25
Pet. ether fraction of MLS13	2.80±0.48***	93.00
$CHCl_3$ fraction of MLS13	60.00±2.00***	85.00
EtOAc fraction of MLS13	15.00±5.20***	62.50
Aqueous fraction of MLS13	12.00±3.70***	70.00
ME of flowers	4.30±2.60***	89.25
ME of stem barks	4.30±1.90***	89.25
Ranitidine	3.00±1.10***	92.50

*(*P<0.05, **P<0.01, *** P<0.001) compared to the control group. Data are presented as mean ± S.E.M in each group. (n = 4) rats in each group*

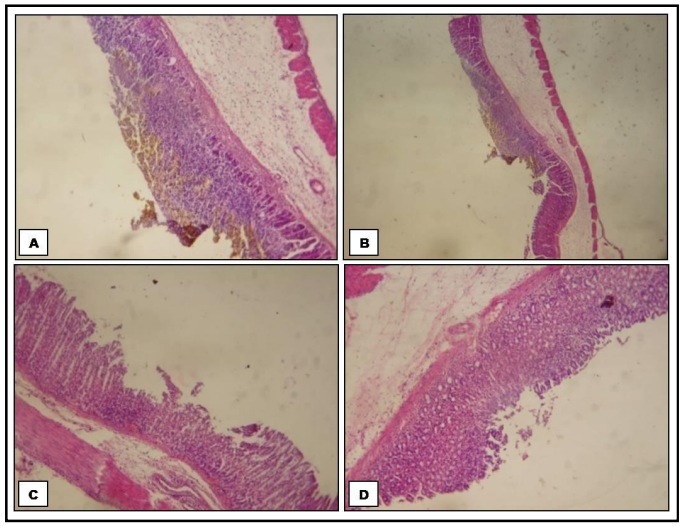

Fig. 1. Histopathological results; A and B-control group, C-pet. ether fraction group and D-ranitidine group

5. CONCLUSION

The present study revealed that *P. cereifera* has various pharmacological effects viz., the ME of MLS13 and stem barks have the highest anti-inflammatory activity in yeast *(***P<0.001)* and carrageenan-indiuced (****P<0.001*) paw edema rats, respectively. Furthermore, both ME of flowers (****P<0.001*) and EtOAc fraction (****P<0.01*) exhibited significant anti-hyperglycemic activity in alloxan-induced diabetic rats. Moreover, pet. ether fraction exhibited the highest gastroprotective activity (****P<0.001*) in indomethacin-induced gastric ulceration rats. Additionally, the current work revealed that ME of *P. cereifera* MLS13 has a wide safety margin. Therefore, this study could be helpful in the development of new drugs.

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CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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