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Original Research Article

Evaluation of Analgesic, CNS Depressant and Antidiarrhoeal Activities of *Psidium guineense* Leaf Extract

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ABSTRACT

Psidium guineense plant had been used as a folk medicine in Bangladesh for ages. The study evaluated the analgesic, central nervous system (CNS) depressant and antidiarrheal effects of aqueous (AEPG), methanol (MEPG) and dichloromethane (DEPG) extracts of the *P. guineense leaves* in mice. The analgesic activity was investigated by acetic acid-induced writhing test and tail immersion test whereas the CNS depressant and the antidiarrheal activity was assessed by hole cross test and magnesium sulphate-induced diarrhea in mice, respectively. The mice were given three doses of each extract (50, 100 and 200 mg/kg body weight) orally and 1% Tween-80 in normal saline (5 mL/kg) was used as control in all experiment. Ibuprofen (10 mg/kg), diazepam (2 mg/kg) and loperamide (10 mg/kg) were used as standard drugs in analgesic, CNS depressant and antidiarrheal tests, respectively. The extracts showed significant ($p < 0.05$) analgesic activity in both tests but DEPG (200 mg/kg) exhibited the maximum analgesic effect, 83.14% inhibition of writhing and 59.34% elongation of tail withdrawal time after 120 minutes. In the hole cross test, AEPG exerted most depressant effect i.e.it reduced 97.64% of the movement of the mice after 120 min. MEPG at a dose of 200mg/kg inhibited diarrhoea by 95% and inhibited defeacation by 79.66%. Based on the results, it can be concluded that the leave extracts of *P. guineense* possess marked analgesic, CNS depressant and antidiarrheal activities in mice.

Keywords: *Psidium guineense*, Analgesic, CNS depressant, Anti-diarrheal.

Introduction

For years, plants have been used as the major source of medicine.[1] Plants with medicinal values are rich in different bioactive compounds and are the biggest source of noble molecules.[2] The diverse pool of bioactive molecules has made traditional system of medicines a force to be reckoned with. Developing as well as developed countries are putting emphasis on new drug discovery from plant sources.[3,4] *Psidium guineense* belonging to the Myrtaceae family, commonly known as Brazilian guava, Castilian guava, Sour guava, Guinea guava,[5] is native to part of America ranging from Mexico to Argentina and some parts of the Caribbean. Later it naturalized in some parts of Indian subcontinent. The plant is a medium-sized tree (grows up to 6-9 meters tall) having a smooth, patchy, peeling whitish brown bark. The leaves are green, simple, alternate, gland dotted, apex ovate having a characteristic aroma. Its flowers are whitish in color and grow singly or in a cluster of 2-3. The fruits are pear-shaped berry (2.5 -10 cm in diameter) having numerous tiny seeds. When ripe, the green fruit turns yellow in color and the flesh color is mostly white or pink. *Psidium guineense* is rich in different types of flavonoids, tannins and isoprenoids.[6] The literature review reveals that it has anti-bacterial, anti-inflammatory, anti-viral, anti-diabetic, anti-proliferative and hepatoprotective activities.[7-12]

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On the basis of traditional uses and scientific work till date our study focused on investigating the analgesic, CNS depressant and anti-diarrheal properties of leaves of *Psidium guineense*.

Materials and Methods

Plant collection

Leaves of the plant were collected from Kotbari, Cumilla, Bangladesh on 20th July, 2019 and were identified at the Bangladesh National Herbarium, Mirpur, Dhaka where the Voucher specimen no: 32766 was deposited.

Drying and grinding

The leaves were dried for 2 days under sunlight and then 7-8 days under shade. The dried leaves are pulverized into a coarse powder using a grinder. The powder was stored in an airtight container and kept in a cool, dark and dry place until further analysis.

Preparation of the extract

The powdered material (500 g) was macerated with 2000 mL distilled water in a clean, flat bottomed glass container. Similarly, same amount of powder (500 g) was macerated in 2000 mL methanol and 2000 mL dichloromethane (DCM), respectively. All the containers with its contents were sealed and kept for a period of 7 days with occasional shaking and stirring. Then, the mixtures were filtered with a piece of clean, white cotton material and further filtered with Whatman filter paper (Bibby RE200, Sterilin Ltd., UK), separately. The filtrates were poured into three different beakers with labeling. Each of the beakers was weighted by an electrical balance. The extracts of methanol and dichloromethane were concentrated at low pressure with a rotator whereas aqueous extract was condensed in a water bath for two days. [13] All the concentrated extracts were kept in a

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refrigerator at 2-8°C. The aqueous, methanol and dichloromethane extracts were labelled as AEPG, MEPG and DEPG, respectively.

Drugs and chemicals

Methanol, dichloromethane (DCM), acetic acid, magnesium sulfate were procured from Merck, Germany and the distilled water was prepared in-house. Ibuprofen, diazepam, loperamide were collected from Square Pharmaceuticals Ltd., Bangladesh. All the chemicals used in these investigations were of analytical reagent grade.

Animals

Swiss-albino mice of either sex aged 4-5 weeks, average weight 25-30 g were used for the experiment. The mice were purchased from the Animal Research Branch of the International Centre for Diarrheal Disease and Research, Bangladesh (ICDDRB). They were kept in a standard environmental condition (at 24.0 ± 0°C temperature & 55-65% relative humidity and 12 hours light-12 hours dark cycle) [14] for one week for acclimation after their purchase and fed ICDDRB formulated rodent feed and water. The experimental protocols were approved by the Ethical Committee of Animal Studies of Comilla University, Cumilla-9208, Bangladesh. The approval number was CoU/PHARM/AEC/15/06/032.

Analgesic Activity

Acetic acid induced writhing test

The peripheral analgesic activity of the extracts was studied by using acetic acid- induced writhing test.[15-17] The animals were divided into eleven groups including control group (Group 1), positive control group (Group 2) and the test groups (Group 3-11). The test samples were given in three dose (50,100 and 200 mg/kg body weight, orally) respectively, with six mice in each group, so the total test group was nine. The control group received vehicle orally (1% Tween-80 in normal saline, 5 mL/kg) and the positive control group received ibuprofen orally at 10 mg/kg body weight as standard. The animals of three test groups were treated with AEPG, MEPG and DEPG, with each extract having three different doses (50,100 and 200 mg/kg body weight, orally) respectively. After 30 minutes of vehicle, ibuprofen and extract administration; 0.6% acetic acid was administered into the peritoneum of each animal. The writhing response, which consisted of a contraction of the abdominal muscle together with a stretching of the hind limbs, was determined for 30 minutes. The percentage reduction of abdominal constriction indicates the percentage protection against the writhes which was taken as an index of analgesia. It was calculated as: % inhibition= $\frac{Nc-Nt}{Nc} \times 100$

Where, N_c = number of writhing of the control group,
N_t = number of writhing of the treated group.

Tail immersion test

Tail immersion test was used to assess the central analgesic activity of *Psidium guineense.*[18, 19] The mice were randomly selected and divided into different groups and treated with AEPG, MEPG and DEPG, with each extract having three different doses (50,100 and 200 mg/kg body weight, orally) respectively. The tail immersion test involved immersing the extreme 3cm of the rat's tail in a water bath containing water at a temperature of (55.0 ± 0.5) °C. After immersing within a few minutes, the rat reacted by withdrawing the tail. The reaction time of the groups was taken at 30 min, 1.0 h, 2.0 h and 3.0 h after a latency period of 30 min following the administration of the tests substances. The cut off time, i.e. time of no response was put at 120 seconds. The results of the tail immersion test are expressed as a percentage of the maximal possible effect (% MPE), which was calculated using the following formula:

$$\% \text{ MPE} = \frac{\text{Post drug latency} - \text{pre drug latency}}{\text{Post drug latency}} \times 100$$

Anxiolytic or Central Nervous System (CNS) Depressant Activity:

Hole cross test

This method is used to evaluate the psychotropic effects of different extracts on the spontaneous locomotor activity of test animals.[20] The hole cross box is a 30 × 20 × 14 cm^3 cage in size with a partition in the middle having a hole of 3 cm diameter with a height of 7.5 cm. The mice were divided into eleven groups. They were treated with vehicle (1% Tween-80 in normal saline, 5 mL/kg), diazepam (2mg/kg bw., orally) and AEPG, MEPG & DEPG of different doses (50,100,200 mg/kg bw., orally) accordingly and placed in the hole cross box. The total number of passages of each mouse through the hole from one chamber to another was counted for a period of 5 min on 0, 30, 60, 90 and 120 min during the study period. CNS depressant activity was assessed by the reduced number of passages of mice through the hole and percentage protection of movement was calculated at 120 min by the following formula. [21]

$$\% \text{ Inhibition} = \frac{No-Ns}{No} \times 100$$

Where,
N_o = the average number of passage by control group,
N_s =the average number of passage by treatment or standard group.

Antidiarrheal Activity

Magnesium sulfate-induced diarrhea in mice

Mice of either sex were kept in fasting condition for 18 hours prior to the experiment which was done according to established method.[22] The animals were divided into eleven groups of six mice each; Group-1 (control) received vehicle (1% Tween-80 in normal saline, 5 mL/kg, Group-2 (positive control) received loperamide orally at 3mg/kg body weight as standard drug. Experimental groups, (group 3, 4 and 5) received aqueous extract, (group 6, 7 and 8) methanol extract and (group 9, 10 and 11) DCM extracts orally at dose 50,100,200 mg/kg body weight respectively; after an hour, each mouse received magnesium sulfate (2 g/kg) via oral route. The animals were placed individually in cages over white filter paper. The number of wet feces was recorded for a period of 4 hours. The activity of each group was expressed as percentage inhibition (%) of defecation and percentage inhibition of diarrhea. It was calculated using the following formula. [23-25]

$$\% \text{ Inhibition} = \frac{No-Ns}{No} \times 100$$

Where,
N_o = the average number of feces by control group,
Ns =the average number of feces by treatment or standard group.

Statistical analysis

Values are expressed as mean ± standard error of mean (SEM). Dunnett's test was performed to calculate statistical significance by one-way analysis of variance (ANOVA). Pair wise comparisons among different treatment groups were done with Post-hoc Tukey test. SPSS software of IBM Corporation, New York, USA (version 16.0) was used for analyzing the data. $P < 0.05$ was considered statistically significant.

Result and Discussion

Analgesic Activity

Acetic acid-induced writhing test

The analgesic effects of the extracts were evaluated though acetic acid induced writhing test in swiss albino mice. All the extracts were found to reduce the writhing response significantly ($p < 0.05$) in comparison to control group and showed dose-dependent reduction the abdominal writhes (Table 1). The positive control (Ibuprofen, 10 mg/kg, p.o.) showed maximum writhing inhibition (92.17%). Among the extracts, DEPG exhibited the most potent analgesic activity (83.14% inhibition of abdominal writhing at 200 mg/kg, p.o.). AEPG and MEPG at a dose of 200 mg/kg showed 61.76% and 78.69% inhibition, respectively. The order of analgesics potential among the three extracts was DEPG > MEPG > AEPG.

Tail immersion test

All the extracts showed potential analgesic activity by prolonging the heat stress tolerance time of treated mice in a dose-dependent fashion

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(Statistically significant; $p < 0.05$) compared to the control group. The reflex time of tail withdrawal of the mouse in hot water was monitored carefully and represented as %MPE in table 2. Ibuprofen used as standard at a dose of 10mg/kg exhibited 44.7% (4.34 ± 0.066), 57.51% (5.78 ± 0.033), 58.43% (6.28 ± 0.044) and 70.07% (9.59 ± 0.091) MPE at 30 min, 60 min and 120 min respectively. Among the extracts DEPG showed the highest %MPE. At a dose of 200 mg/kg, DEPG showed 38.77% (3.92 ± 0.02), 48.53% (4.78 ± 0.040), 52.91% (4.78 ± 0.040) and 59.34% (7.06 ± 0.014) MPE at 30 min, 60 min, 90 min and 120 min respectively. The overall order of tail withdrawal reflex time of the extracts was: DEPG > MEPG > AEPG.

CNS Depressant Activity

Hole cross test

Table 3 presents the data regarding hole cross test. All the mice treated with diazepam or extract showed a significant decrease ($p < 0.05$) in the number of passes through the hole. Diazepam (2mg/kg) showed 87.51%, 87.84%, 94.32%, 85.71% inhibition at 30 min, 60 min, 90 min and 120 min respectively. Whereas, AEPG (200mg/kg) showed 94.64%, 95.09%, 97.16% and 97.64% inhibition, respectively. The order of reduction of hole crossing was AEPG > DEPG > MEPG.

Antidiarrheal Activity

Magnesium sulfate-induced diarrhea in mice

The results of the effect of *Psidium guineense* on magnesium sulfate-induced diarrhoea are shown in Table-4. At 50,100,200 mg/kg, all the extracts showed statistically significant ($p < 0.05$) inhibition of diarrhea in comparison with the control. After four hours, loperamide (10mg/kg) showed 80% and 84.98% inhibition of diarrhea respectively. The corresponding values for AEPG, MEPG and DEPG (200 mg/kg each) are 60% and 90.09%, 79.66% & 95% and 60% and 85.70% respectively. So the observed order of inhibition of defecation and diarrhea is MEPG > AEPG > DEPG.

The study was evaluated the analgesic, CNS depressant and antidiarrheal activities of *Psidium guineense* leave extracts in Swiss mice model. The results are presented in Tables 1-4.

Table 1: Analgesic effects of *Psidium guineense* leaf extracts and ibuprofen in acetic acid-induced writing test

Treatment	Dose	No. of writhing	% inhibition
Control	5 mL/kg	14.83 ± 0.440 $^{\theta}$	00
Standard (ibuprofen)	10 mg/kg	1.17 ± 0.440*	92.17
AEPG	50 mg/kg	7.17 ± 0.440* $^{\theta}$	51.65
AEPG	100 mg/kg	6.17 ± 0.726* $^{\theta}$	58.39
AEPG	200 mg/kg	5.67 ± 0.927* $^{\theta}$	61.76
MEPG	50 mg/kg	7.67 ± 0.166* $^{\theta}$	48.28
MEPG	100 mg/kg	5.50 ± 1.763* $^{\theta}$	62.91
MEPG	200 mg/kg	3.17 ± 0.167*	78.69
DEPG	50 mg/kg	3.83 ± 0.167*	74.17
DEPG	100 mg/kg	3.17 ± 0.440*	78.79
DEPG	200 mg/kg	2.50 ± 0.288*	83.14

Data are means of 6 animals ± SEM (Standard error mean); * $p < 0.05$ vs. Control (Dunnett's t test); $^{\theta}$ $p < 0.05$ vs. Standard; pair-wise comparison by Post-hoc Tukey test.

Table 2: Analgesic effect of *Psidium guineense* leaf extracts and ibuprofen in tail immersion test

Treatment	Dose	Response time (s) (%MPE)				
		0 min	30 min	60 min	90 min	120 min
Control	5 mL/kg	2.45 ± 0.097	2.40 ± 0.083 $^{\theta}$	2.46 ± 0.036 $^{\theta}$	2.58 ± 0.037 $^{\theta}$	2.87 ± 0.032 $^{\theta}$
Standard (Ibuprofen)	10 mg/kg	2.30 ± 0.074	4.34 ± 0.066* (44.7)	5.78 ± 0.033* (57.51)	6.28 ± 0.044* (58.43)	9.59 ± 0.091* (70.07)
AEPG	50 mg/kg	2.34 ± 0.07	2.95 ± 0.041* $^{\theta}$ (18.64)	3.48 ± 0.105 (29.31)	4.92 ± 0.015*$^{\theta}$ (47.56)	4.95 ± 0.015*$^{\theta}$ (42.02)
AEPG	100 mg/kg	2.18 ± 0.043*	3.49 ± 0.015 *$^{\theta}$ (31.23)	4.20 ± 0.078*$^{\theta}$ (41.42)	4.49 ± 0.02*$^{\theta}$ (42.53)	5.28 ± 0.015*θ (45.64)
AEPG	200 mg/kg	2.40 ± 0.055	3.84 ± 0.032* $^{\theta}$ (37.5)	4.35 ± 0.021*$^{\theta}$ (43.44)	4.96 ± 0.0115*$^{\theta}$ (47.98)	5.87 ± 0.305*$^{\theta}$ (51.11)
MEPG	50 mg/kg	2.15 ± 0.026*	2.95 ± 0.017* $^{\theta}$ (18.64)	3.78 ± 0.026*$^{\theta}$ (34.92)	4.56 ± 0.026*$^{\theta}$ (43.42)	5.46 ± 0.028*$^{\theta}$ (47.43)
MEPG	100 mg/kg	2.95 ± 0.017* $^{\theta}$	3.60 ± 0.015* $^{\theta}$ (33.33)	4.07 ± 0.026*$^{\theta}$ (39.56)	4.99 ± 0.005*$^{\theta}$ (48.29)	5.77 ± 0.066*$^{\theta}$ (50.25)
MEPG	200 mg/kg	2.79 ± 0.026* $^{\theta}$	3.58 ± 0.032* $^{\theta}$ (32.96)	4.85 ± 0.026* $^{\theta}$ (49.27)	5.42 ± 0.0152*$^{\theta}$ (52.39)	6.12 ± 0.014*$^{\theta}$ (53.10)
DEPG	50 mg/kg	2.09 ± 0.034*	3.03 ± 0.005* $^{\theta}$ (20.79)	3.98 ± 0.017* $^{\theta}$ (38.19)	5.05 ± 0.0152*$^{\theta}$ (48.91)	5.92 ± 0.035*$^{\theta}$ (51.52)
DEPG	100 mg/kg	2.07 ± 0.115*	3.48 ± 0.037* $^{\theta}$ (31.03)	4.10 ± 0.035* $^{\theta}$ (40.01)	5.25 ± 0.02*$^{\theta}$ (50.85)	6.07 ± 0.055*$^{\theta}$ (52.71)
DEPG	200 mg/kg	2.15 ± 0.023*	3.92 ± 0.02* $^{\theta}$ (38.77)	4.78 ± 0.040* $^{\theta}$ (48.53)	5.48 ± 0.041*$^{\theta}$ (52.91)	7.06 ± 0.014*$^{\theta}$ (59.34)

Data are means of 6 animals ± SEM (Standard error mean); * $p < 0.05$ vs. Control (Dunnett's t test); $^{\theta}$ $p < 0.05$ vs. Standard; pair-wise comparison by Post-hoc Tukey test.

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Table 3: Anxiolytic effects of *Psidium guineense* leaf extracts and diazepam in hole cross test

Sample	Dose	Number of hole crossing (% reduction)				
		0 min	30 min	60 min	90 min	120 min
Control	5 mL/kg	7.66 ± 0.33$^{\theta}$	18.66 ± 0.881$^{\theta}$	13.66 ± 0.881$^{\theta}$	11.66 ± 0.881$^{\theta}$	14 ± 1.154$^{\theta}$
Standard (diazepam)	2 mg/kg	0.33 ± 0.33*	2.33 ± 0.33* (87.51)	1.66 ± 0.33* (87.84)	0.66 ± 0.66* (94.32)	2 ± 1.154* (85.71)
AEPG	50 mg/kg	1.33 ± 0.66*	1.00 ± 0.577* (94.64)	0.666 ± 0.666* (95.16)	0.333 ± 0.333* (97.14)	0.333 ± 0.333* (97.62)
AEPG	100 mg/kg	1.33 ± 0.66*	1.00 ± 0.577* (94.64)	0.666 ± 0.666* (95.16)	0.67 ± 0.33* (94.25)	0.33 ± 0.33* (97.64)
AEPG	200 mg/kg	1 ± 0.577*	0.666 ± 0.666* (96.44)	0.67 ± 0.33* (95.09)	0.33 ± 0.33* (97.16)	0.33 ± 0.33* (97.64)
MEPG	50 mg/kg	5.00 ± 0.577 $^{\theta}$	3.66 ± 1.154* (80.38)	6 ± 0.577* $^{\theta}$ (56.07)	6.67 ± 0.881*$^{\theta}$ (47.29)	7 ± 0.577*$^{\theta}$ (50)
MEPG	100 mg/kg	5.33 ± 0.881 $^{\theta}$	2.00 ± 0.88* (80.38)	1.66 ± 1.201* (65.88)	2.00 ± 0.577* (60.03)	3.33 ± 0.881* (76.21)
MEPG	200 mg/kg	3.66 ± 1.201*	1.67 ± 0.881* (91.05)	2 ± 0.577* (85.35)	1.33 ± 0.33* (88.59)	2.33 ± 0.881* (83.35)
DEPG	50 mg/kg	0.66 ± 0.333*	2 ± 0.577* (53.81)	2.67 ± 0.881* (67.94)	3.67 ± 0.881* (31.14)	1.67 ± 0.33* (78.19)
DEPG	100 mg/kg	1.66 ± 0.881*	1 ± 0.577* (76.90)	1.67 ± 0.33* (79.95)	1 ± 0.577* (81.23)	1 ± 0.577* (86.94)
DEPG	200 mg/kg	1.33 ± 0.33*	1 ± 0* (76.90)	0.666 ± 0.666* (87.99)	0.333 ± 0.333* (87.61)	0.67 ± 0.33* (91.25)

Data are means of 6 animals ± SEM (Standard error mean); * $p < 0.05$ vs. Control (Dunnett's t test); θ $p < 0.05$ vs. Standard; pair-wise comparison by Post-hoc Tukey test.

Table 4: Antidiarrheal effects of *Psidium guineense* leaf extracts on $MgSO_4$ induced diarrhea test in mice

Treatment	Dose	Total number of feces (Mean ± SEM)	% Inhibition of defecation	Total number of diarrheal feces (Mean ± SEM)	% Inhibition of diarrhea
Control	5 mL/kg	20 ± 1.154$^{\theta}$	00	6.66 ± 0.881$^{\theta}$	00
Standard Loperamide	10 mg/kg	4 ± 0.577*	80	1.00 ± 0.577*	84.98
AEPG	50 mg/kg	12 ± 1.154* $^{\theta}$	40	1.33 ± 0.88*	80.03
AEPG	100 mg/kg	8 ± 0.577* $^{\theta}$	60	1 ± 0.577*	84.98
AEPG	200 mg/kg	8 ± 0.577* $^{\theta}$	60	0.66 ± 0.66*	90.09
MEPG	50 mg/kg	9 ± 1.154* $^{\theta}$	55	0.66 ± 0.333*	80.03
MEPG	100 mg/kg	4.667 ± 0.333*	76.66	0.66 ± 0.333*	89.98
MEPG	200 mg/kg	2.667 ± 0.666*	79.66	0.33 ± 0.333*	95
DEPG	50 mg/kg	6 ± 0.577*	40	0.66 ± 0.333*	57.08
DEPG	100 mg/kg	5 ± 0.577*	50	0.667 ± 0.666*	71.37
DEPG	200 mg/kg	4 ± 0.577*	60	0.333 ± 0.333*	85.70

Data are means of 6 animals ± SEM (Standard error mean); * $p < 0.05$ vs. Control (Dunnett's t test); $^{\theta}$ $p < 0.05$ vs. Standard; pair-wise comparison by Post-hoc Tukey test.

The analgesic effect of a drug is commonly evaluated by measuring the anti-analgesic activities in response to an external stimulus. The stimulus may be thermal, chemical or mechanical.[26] Acetic acid causes the release of endogenous arachidonic acid from tissue phospholipid and eventually triggers the prostaglandin biosynthesis pathway.[27] This local inflammatory response leads to an abnormal writhing response. The extracts of *P. guineense* leaves were shown to significantly ($p < 0.05$) decreased the writhing response. This could be attributed to the inhibition of prostaglandin biosynthesis, a peripheral mechanism.[28] On the other hand, the tail immersion test indicates the central analgesic effect of a drug or extract. [29] From table 2, we can see that all the extracts increased the latent period significantly. This is possibly a spinal reflex of μ2-and δ-opioid receptors by morphine-like drugs which selectively prolongs the reaction time of tail withdrawal of the treated mice. [30]

The evaluation of locomotor activity is a good indicative means of assessing a drug's action on CNS. Movement of test animals is related proportionally to the level of excitability of the CNS and any reduction on that might be as a result of CNS depression.[31,32] The extracts significantly ($p < 0.05$) decreased the movement through the hole which is indicative of their CNS depressant effect. The effect may be a result of potentiation of GABAergic inhibition followed by membrane hyperpolarization. This probably causes a drop in the firing rate of critical neurons in CNS and/or activates the GABA receptor. Literature survey revealed that many phytochemicals (like flavonoids and steroids) act as ligands for GABA receptors and may cause allosteric modification like benzodiazepines do. [32,33] So, CNS depressant effects may be due to the phytoconstituents of *P. guineense* extracts. The extracts showed marked antidiarrheal activity. Magnesium sulfate causes secretion of cholecystokinin from duodenal mucosa and increases peristaltic movement. This in turn reduces the absorption of water and sodium from GIT and results in diarrhea. Pretreatment with the *P. guinennse* extracts significantly reduced diarrhea caused by magnesium sulfate.

Conclusion

The study demonstrated analgesic, CNS depressant and antidiarrheal activity of *P. guineense* leaves extract. Phytoconstituents like flavonoids, tannins and isoprenoids might be responsible for these activities.

Conflict of interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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