ABSTRACT
To evaluate the anticonvulsant, CNS depressant and antinociceptive properties of corm extract of *Musa paradisiaca* cv. Puttabale on *in vivo* models. The quantification and identification of phenolics and flavonoids were determined in crude extract using HPLC-UV analysis. The LD$_{50}$ was determined and extracts were used at doses of 100, 200 and 300 mg/kg for the studies. The anticonvulsant activity was evaluated using Maximum electroshock (MES), Pentylentetrazole (PTZ) and locomotor test. For the evaluation of CNS depressant properties, forced swim test, muscle co-ordination test and antinociceptive action of abdominal writhing, tail-flick test, thermal-induced pain models were used in experiments. The extract depicted total phenolics (628.6 μg/mg) and flavonoids (321.6 μg/mg) and caused a significant reduction of MES (4.33 ± 0.49), PTZ (168.83 ± 1.49) and locomotor test (129.33 ± 1.43). The extract also reduced the reaction time of forced swim test (59.50 ± 1.34) and muscle co-ordination test (89.32%). As well, extract reduced significantly nociception induced by acetic acid (65%), tail-flick test (90 min) and hot plate (180 min). The results suggest that the corm extract of *M. paradisiaca* cv. Puttabale possess anticonvulsant, CNS depressant and antinociceptive properties which may be attributable to the presence of phenolics and flavonoids in the plant.
Key words: *Musa paradisiaca* cv. Puttabale, corm ethanol extract, Maximum electroshock, Pentyleneetetrazole, Forced swim test, Muscle co-ordination test, acetic acid-induced writhing.

INTRODUCTION

*Musa paradisiaca* L. (Musaceae) cultivar Puttabale is an indigenous banana commonly cultivated in the Malnad region of Karnataka and distributed in Assam, Madhya Pradesh, Bihar, Gujarat, Andhra Pradesh, Jalgaon district (Maharashtra), West Bengal, and Tamil Nadu[1]. The fruits are valued for delicious taste. Traditionally, the plant parts like fruits, stem juice, flower juice have been used for treatment such as abscess, alopecia (female), anasarca, pain reliever, cooling effect on burns, cancer, cataplasm, diabetes, diarrhea, dog bites, dysentery, dyspepsia, cramps, fractures, gangrene, headache, hematuria, hemiplegia, hemoptysis, hemorrhage, hypertension, lizard bites, mange, marasmus, migraine, nausea, otalgia, psoriasis, ringworm, scorpion sting, septicemia, shingles, smallpox, snake bite, sore, strain, syphilis, tuberculosis, warts, and wound[2]. The pharmacological investigation of banana fruits, stem juice, flowers revealed for antidiarrhoeal activity[3,4], antidiabetic[5], antilithic[6], antiulcerative activity[7-9], antimicrobial activity[10-15], hypoglycemic activity[16-19], hypocholesterolaemic activity[20], antioxidant activity[21,22], wound healing activity[23], anti-allergic activity[24], antimalarial activity[25], anti-snake venom activity[26] and analgesic activity[27,28].

Literature survey revealed that the unripe banana fruits have anticonvulsant activity[29] and the analgesic activity from stem & leaves extracts of *Musa paradisiaca*[30]. Since, corm ethanol extract of *Musa paradisiaca* (L.) Puttabale have the presence of flavonoids, glycosides, terpenoids and tannins[31,32]. Various classes of phytoconstituents such as alkaloids, terpenes, triterpenoids, and flavonoids have been reported as an anticonvulsant, analgesic activity[33-39]. Hence, this study was undertaken to evaluate anticonvulsant, antidepressant and analgesic properties.

MATERIALS AND METHODS

Collection and Preparation of the plant extraction

The corms of *M. paradisiaca* cv. Puttabale were collected from the farmyard region of the Western Ghats, Karnataka, India. The corm of cultivar Puttabale was washed thoroughly in tap water to remove soil particles and other contaminates, followed by distilled water. It is then shade dried, grind coarsely by using mechanical blender and passes through 40-mesh sieve. About 1 kg of powder material was dipped in cold 95% ethanol and incubated on
rotary shaker at 80-120 rpm for 15 days in room temperature. The extracts were filtered and concentrated in vacuum under reduced pressure using rotary flash evaporator (Buchi, Flawil, Switzerland) and then the extract was kept on water bath to obtain crude extract and finally vacuum dried. The corm extract were dissolved in water and subjected to phytochemical screening.

**Determination of total phenol content**

Total phenol content in corm ethanol extract was measured by the Folin–Ciocalteu method\(^4\). 1 ml of crude extract (50 µg) was mixed with 0.5 ml of Folin–Ciocalteu reagent and 7.5 ml deionized water. The mixture was kept at room temperature for 10 min, and then 1.5 mL of 20% (w/v) sodium carbonate added. The mixture was heated in a water bath at 40°C for 20 min and then cooled in an ice bath. Absorbance was measured against the blank at 765 nm using a UV-visible spectrophotometer (Shimadzu UV-1601PC, Tokyo, Japan). An amount of total phenolic was expressed in terms of equivalent to gallic acid (µg/mg of dry mass).

**Determination of total flavonoid content**

Estimation of flavonoid contents of 95% ethanol extract of *M. paradisiaca* cv. Puttabale was carried out adopting the method described by Zhishen et al.,\(^{41}\) (1999). 5 ml of extract (100 µg) was mixed with 0.3 ml of 5% sodium nitrite was added and mixed well. After 5 min at room temperature, 0.6 ml of 10% aluminium chloride was added. After 6 min, 2 ml of 1 M sodium hydroxide was added. The total flavonoid content was expressed in mg of catechin equivalents (CE) per gram of extract. (±)-catechin was used for constructing the standard curve and the results were expressed as µg of (±)-catechin equivalents (CE) per mg of extract.

**HPLC–UV analysis**

Phenolic acids and flavonoids from crude ethanol extract were analyzed by HPLC (Model LC-10ATVP. Shimadzu Corp, Kyoto, Japan) on a reversed phase Shimpak C18 column (5 µm, 250 mm × 4.6 mm). Phenolic content in crude extract were detected using octade-cylsilyl silica gel as stationary phase. Solvent system consisting of [A] phosphoric acid:water (0.5:99.5, v/v), [B] acetonitrile was used as mobile phase at a flow rate of 1 ml/min. Phenolic acid standards such as gallic acid, p-coumaric acid, ellagic acid and hydroxyl benzoic acid were employed for identification of phenolic acids present in ethanol extract by comparing the retention time under similar experimental conditions. The detector used for analysis was UV detector at 220 nm. Flavonoid content in extract was detected using octadecylsilyl silica
gel as stationary phase. Solvent system consisting of methanol, water and phosphoric acid (50:49.6:0.4, v/v) was used as mobile phase at a flow rate of 0.5 ml/min. Rutin, quercetin, myricetin, kaempferol, luteolin were used as reference standard to identify the flavonoids in ethanol extract.\(^\text{[42]}\)

**SCREENING OF PHARMACOLOGICAL PROPERTIES**

**Experimental animals**

Swiss albino mice of either sex weighing 25-30 g were procured from Central Animal House, National College of Pharmacy, Shivamogga, Karnataka, India and were maintained at standard housing conditions (Temp. 23 ± 2°C, humidity 55–60% with a 12 h light and dark cycle). The animals were fed with commercial diet (Durga Feeds and Foods, Bangalore) and water *ad libitum* during the experiment. Animals were fasted, but allowed for water 12 h prior to the experiment. The Institutional Animal Ethical Committee (Ref: NCP/IAEC/CL/12/12/2010-11) permitted the study.

**Acute toxicity study**

The staircase method\(^\text{[43]}\) was adopted for the determination of the acute toxicity. Healthy albino mice of either sex weighing 25-30g were used to determine the safer dose. Water was used as a vehicle to dissolve the extract and was administered orally.

**ANTICONVULSANT ACTIVITY**

**Maximum Electroshock (MES)**

The experimental animals were divided into five groups of six mice each. Group I (control) received normal saline [1ml/mice, per oral (p.o)], Group II received standard drug Phenytoin [25 mg/kg, Intraperitoneal (i.p)] and Group III, IV & V received 100, 200, 300 mg/kg, p.o of ethanol extract, 1 h prior to the induction of convulsions respectively. Maximal electroshock of 150 mA current for 0.2 seconds was administered through ear electrodes to induce convulsion in all the experimental animals.\(^\text{[44]}\) The severity of convulsions was evaluated by observing for 30 min from the time of electric shock for different phases of tonic flexion, tonic extensor, clonus, stupor and compared with control and standard.

**Pentylenetetrazole (PTZ) activity**

The experimental animals were divided into five groups of six mice\(^\text{[45]}\). Group I (control) received normal saline (1ml/mice, p.o), Group II received standard drug diazepam (5 mg/kg, i.p) and Group III, IV & V received 100, 200, 300 mg/kg p.o of ethanol extract. PTZ (60 mg
kg\(^{-1}\)) was injected intraperitoneally to extract treated and control groups after 1 h and animals were kept in individual plastic cages to observe convulsions.

**Locomotor activity**

The locomotor activity was measured using an actophotometer. Each animal were acclimatized with environment and placed individually in an actophotometer for 10 min and a basal activity score was obtained. Subsequently animals were divided into five groups of six mice each. All the groups except Group II were treated as per MES induced seizure model and was received diazepam (1 mg/kg, i.p.). Group III, IV & V received 100, 200, 300 mg/kg p.o of ethanol extract respectively. After 30 min, the activity score was recorded\[^{46}\]. The percentage reduction in locomotor activity was calculated.

**CNS DEPRESSANT ACTIVITY**

The animals were acclimatized one hour before for behavioral tests. 1 h time interval between drug administration and behavioral tests were maintained during oral administrations. The animals were divided into five groups of six mice each. Group I was maintained as control group and received 2% Dimethylsulfoxide (DMSO) in distilled water, orally. Group II maintained as standard and received imipramine commercial drug (M/s. Alkem Ltd. Mumbai) for forced swim test at the dose of 10 mg/kg and chlorpromazine hydrochloride (10 mg/kg) (FLUDAC®, Cadila Pharmaceuticals, Ahmedabad, India) for rotarod test, orally. Group III, IV and V animals were administered with ethanol extract in 2% DMSO at the dose of 100, 200 and 300 mg/kg, orally.

**Forced swim test**

Forced swim test, the most frequently used behavioral model for screening CNS depressant like activity in rodents as proposed by Porsolt et al.,\[^{47}\] (1977). The procedure was same as followed previously. Mice were individually forced to swim in open glass chamber (25 × 15 × 25 cm) containing fresh water to a height of 15 cm and maintained at 26 ± 1°C. At this height of water, animals were not able to support themselves by touching the bottom or the side walls of the chamber with their hind paws or tail. Water in the chamber was changed after subjecting each animal. Each animal showed vigorous movement during initial 2 min period of the test. The duration of immobility was manually recorded during the next 4 min of the total 6 minutes testing period. Mice were considered to be immobile when they ceased struggling and remained floating motionless in water, making only those movements
necessary to keep their head above water. Following swimming session, mice were towel dried and returned to their housing conditions\(^{[48,49]}\).

**Muscle co-ordination test**
This test was carried out using rotarod apparatus. The rotarod apparatus consists of a metal rod (3 cm diameter) coated with rubber attached to a motor with the speed adjusted to 20 rotations per minutes. The rod was 45 cm in length and is divided into 3 sections by metallic discs, allowing the simultaneous test of 3 mice. The rod is in a height of about 50 cm above the table top in order to discourage the animals from jumping off the roller. Cages below the section serve to restrict the movements of the animals when they fall from the roller Swiss albino mice underwent a pretest on the apparatus. Only those animals, which had demonstrated their ability to remain on the revolving rod (20 rpm) for 5 min, were used for the test. The animals were treated in the same way as mentioned under inclined plane test\(^{[47]}\).

**ANTINOCICEPTIVE ACTIVITY**

**Acetic acid-induced writhing test**
Antinociceptive activity was evaluated using the acetic acid-induced abdominal writhing method\(^{[50]}\). Mice were divided into five groups of six animals each. The group I served as control and was treated with 0.6% acetic acid (10 ml/kg) intraperitoneally. After 5 min of injection of acetic acid, number of writhes was counted for 20 min. The group II was administered the drug acetyl salicylic acid (100 mg/kg) and used as standard for the comparison of analgesic activity. The animals of the III, IV & V groups were administered orally with the water dissolved ethanol extract in three different concentrations 100, 200 and 300 mg/kg body weight respectively. The crude extract and the standard drug were treated 1 h before administration of acetic acid. After one hour incubation of all the groups except group I animals were administered with acetic acid. After 5 min, each group mice were observed for the onset of writhing and the number of writhing responses for duration of 20 min. The mean value for each group was calculated and compared with the control.

**Tail flick method**
Swiss albino mice of either sex weighing between 20 to 25 g were evaluated using the tail flick method described by Sewell et al.,\(^{[51]}\) (1976). Mice were divided into five groups of six animals each. The group I served as control and received only normal saline (10 ml/kg); the group II was administered standard drug acetyl salicylic acid (100 mg/kg, p.o). The animals of the III, IV & V groups were treated with ethanol extract in three different concentrations
100, 200 and 300 mg/kg, p.o body weight respectively. One to two centimeter of the tail of experimental mice was immersed in warm water kept constant at 50°C. The pain reaction time was the time taken by the mice to deflect their tails. The first reading is discarded and the reaction time was taken as a mean of the next two readings. A cut off time of 10 sec was observed to prevent any tissue damage to the animal. The latency period (reaction time) was noted when the animal responded with a sudden and characteristic flick or tail lifting. The latent period of the tail-flick response was taken as the index of antinociceptive activity and the tail flick latencies were recorded at pre-drug, 15, 30, 45, 60, 90, 120, 150 and 180 min after administration of drugs.

**Hot plate method**

Swiss albino mice of either sex weighing 20-25 g were divided into five groups each containing six animals. The hot plate was maintained at 55° to 56°C. The animals are placed on the hot plate and the time until either licking or jumping occurs is recorded by a stopwatch. The latency was recorded at 15, 30, 45, 60, 90, 120, 150 and 180 min intervals after standard drug (Aspirin 100 mg/kg) and ethanol extract of three different concentrations 100, 200 and 300 mg/kg body weight respectively. The test was terminated at 15 sec. to prevent tissue damage.[52]

**Statistical analysis**

The data of antinociceptive activity was expressed as mean ± S.E.M of six animals in each group. The statistical analysis was carried out using one way ANOVA followed by Tukey’s t-test. The difference in values at p≤ 0.01 was considered as statistically significant.

**RESULTS**

**Quantitative determination of extract**

The preliminary phytochemical analysis of corm ethanol extract revealed the presence of various phenolic acid, flavonoids, glycosides, terpenoids and tannins (Venkatesh et al., 2013). Total phenolic content in extracts was expressed as equivalent to Gallic acid (EGA) and is found to be 628.6 µg/mg of dry extract. Analysis of flavonoid content was found to be 321.6 µg/mg of dry extract.

**HPLC–UV analysis extract**

The presence of phenolics and flavonoids has been considered as important for medicinal plant to evaluate antinociceptive and anticonvulsant properties.[53,54] HPLC-UV analysis
revealed the presence of Gallic acid, coumaric acid, ellagic, hydroxy benzoic acid and eight unknown peaks in the ethanol extract, which were detected at 220 nm (Fig.1) with retention times of 2.4, 2.9, 4.1 and 8.0, respectively. Among them, gallic acid was the most abundant (529.7 mg/g) phenolic constituent present in ethanol extract.

Figure 1: RP-HPLC chromatogram of phenolic acids of corm ethanol extract of *Musa paradisiaca* cv. Puttabale.

The UV spectral peaks of ethanol extract at 350 nm showed the presence of standard flavonoids such as rutin, quercetin, myricetin, kaempferol and luteolin with retention time 2.0, 2.5, 4.0, 7.0 and 9.0 respectively (Fig. 2). Quercetin was found to be the most abundant flavonoid in the ethanol extract with the concentration of 490.0 mg/g. The presence of various molecules was responsible for the protective activity of corm ethanol extract of *Musa paradisiaca* cv. Puttabale (Table 1).

Figure 2: RP-HPLC chromatogram of flavonoids from corm ethanol extract of *Musa paradisiaca* cv. Puttabale.
Table 1: Quantitative HPLC analysis of phenolic acids and flavonoids in corm ethanol extract

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Phenolic acids (Standard)</th>
<th>Corm ethanol extract of M. paradisiaca cv. Puttabale (mg/g)</th>
<th>Flavonoids (Standard)</th>
<th>Corm ethanol extract of M. paradisiaca cv. Puttabale (mg/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Gallic acid</td>
<td>529.7</td>
<td>Rutin</td>
<td>93.0</td>
</tr>
<tr>
<td>02</td>
<td>Coumaric acid</td>
<td>515.0</td>
<td>Quercetin</td>
<td>490.0</td>
</tr>
<tr>
<td>03</td>
<td>Ellagic acid</td>
<td>277.0</td>
<td>Myricetin</td>
<td>2.0</td>
</tr>
<tr>
<td>04</td>
<td>Hydroxy acid</td>
<td>550.0</td>
<td>Kaempferol</td>
<td>10.0</td>
</tr>
<tr>
<td>05</td>
<td>Benzoic acid</td>
<td>---</td>
<td>Luteolin</td>
<td>3.0</td>
</tr>
</tbody>
</table>

Quantitative estimation of phenolic acids and flavonoids in corm ethanol extract of Musa paradisiaca cv. Puttabale was expressed in milligram per gram of samples.

Acute toxicity study

After 72 h observation, a plot of mortality values versus log dose showed that the LD$_{50}$ of ethanol extract was 3000 mg/kg did not show any sign of mortality. One tenth of this dose was considered as safer dose (300 mg/kg) for administration.

Table 2: Anticonvulsant activity by Maximum Electroshock (MES) induced seizure model

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Treatment Time (sec) in Various Phases of Convulsions (Mean±SEM)</th>
<th>Death/Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Control (MES) (Saline, 1 ml/kg, p.o)</td>
<td>3.17±0.48</td>
<td>9.83±0.48</td>
</tr>
<tr>
<td>II</td>
<td>Standard Drug Phenytoin (25 mg/kg, i.p)</td>
<td>1.17±0.31**</td>
<td>4.00±0.58**</td>
</tr>
<tr>
<td>III</td>
<td>Ethanol Extract (100 mg/kg p.o)</td>
<td>5.17±0.48**</td>
<td>8.17±0.60(ns)</td>
</tr>
<tr>
<td>IV</td>
<td>Ethanol Extract (200 mg/kg p.o)</td>
<td>3.67±0.49(ns)</td>
<td>6.17±0.65**</td>
</tr>
<tr>
<td>V</td>
<td>Ethanol Extract (300 mg/kg p.o)</td>
<td>2.50±0.43(ns)</td>
<td>4.33±0.49**</td>
</tr>
</tbody>
</table>

Values are the mean ± SEM, SEM = standard error of the mean (n = 6). Symbols represent statistical significance.* p < 0.05, ** p < 0.01, as compared to control group. ns = Not Significant.
ANTICONVULSANT ACTIVITY

MES activity
The MES is a standard method to evaluate the chemicals or phytoconstituents capability to protect against hind limb tonic extension (HLTE) and to inhibit seizure discharge within the brain stem substrate. Since, the corm ethanol extract of *M. paradisiaca* cv. Puttabale significantly reduced the duration of HLTE phase at the doses 100 mg (8.17±0.60), 200 mg (6.17±0.65) and 300 mg/kg (4.33±0.49) respectively as compared to the Standard drug phenytoin (4.00±0.58) and control (9.83 ± 0.48) (Table 2). This result showed that may be effective as an anticonvulsant by different constituents of crude extract.

Locomotor activity
Locomotor activity is measured as a log of alertness and decreases due to reduce in dopaminergic transmission and consequently increase in GABAergic\[^{[55,56]}\]. The corm ethanol extracts of *M. paradisiaca* cv. Puttabale decrease the locomotion in dose-dependent manner of 100 mg (459.83±2.68), 200 mg (245.83±2.17) and 300 mg/kg (129.33±1.43) as compared to standard drug Diazepam (104.50±1.75) and control (461.17±3.09). The protection against the mortality of corm extract is 13.80%, 54.12%, and 75.58% (Table 4) supporting the earlier evidence\[^{[57]}\].

### Table 3: Anticonvulsant activity by Pentylenetetrazole (PTZ) induced seizure model

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Onset of convolution (s)</th>
<th>Duration of convolution (s)</th>
<th>Number of animals recovered</th>
<th>Protection against Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Control (PTZ) (Saline, 1 ml/kg, p.o)</td>
<td>126.67±2.01</td>
<td>868.00±2.77</td>
<td>0/6</td>
<td>0.00</td>
</tr>
<tr>
<td>II</td>
<td>Standard Drug Diazepam (5 mg/kg, i.p)</td>
<td>0.00±0.00**</td>
<td>0.00±0.00**</td>
<td>6/6</td>
<td>100.00</td>
</tr>
<tr>
<td>III</td>
<td>Ethanol Extract (100 mg/kg p.o)</td>
<td>164.00±1.88**</td>
<td>709.17±1.58**</td>
<td>2/6</td>
<td>33.33</td>
</tr>
<tr>
<td>IV</td>
<td>Ethanol Extract (200 mg/kg p.o)</td>
<td>145.17±2.34**</td>
<td>441.17±2.33**</td>
<td>4/6</td>
<td>66.66</td>
</tr>
<tr>
<td>V</td>
<td>Ethanol Extract (300 mg/kg p.o)</td>
<td>170.83±2.12**</td>
<td>168.83±1.49**</td>
<td>5/6</td>
<td>83.33</td>
</tr>
</tbody>
</table>

*Values are the mean ± SEM, SEM = standard error of the mean (n = 6), Symbols represent statistical significance. \* p < 0.05, \** p < 0.01, as compared to control group. ns = Not Significant.*
PTZ activity

The administration of *M. paradisiaca* cv. Puttabale ethanolic extracts at doses of 100 mg (709.17±1.58), 200 mg (441.17±2.33) and 300 mg/kg b.w. (168.83±1.49), 1 hr prior to the injection of PTZ, significantly (p<0.01) delayed the onset of convulsions with 33%, 66.6% and 83.3% protection. The standard drug Diazepam in a dose of 5 mg kg\(^{-1}\) b.w. totally abolished the episodes of convulsions with 100.0% protection as compared to control (868.00±2.77) and crude extract (Table 3).

Table 4: Anticonvulsant activity by locomotor activity

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Locomotor activity (score) in 10 min</th>
<th>Protection against Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Before treatment Mean±SEM</td>
<td>After treatment Mean±SEM</td>
</tr>
<tr>
<td>I</td>
<td>Control (MES)</td>
<td>535.33±2.76</td>
<td>461.17±3.09</td>
</tr>
<tr>
<td>II</td>
<td>Standard Drug (5 mg/kg, i.p)</td>
<td>533.50±2.05</td>
<td>104.50±1.75</td>
</tr>
<tr>
<td>III</td>
<td>Diazepam Ethanol Extract (100 mg/kg p.o)</td>
<td>533.50±1.26</td>
<td>459.83±2.68</td>
</tr>
<tr>
<td>IV</td>
<td>Ethanol Extract (200 mg/kg p.o)</td>
<td>535.83±1.17</td>
<td>245.83±2.17</td>
</tr>
<tr>
<td>V</td>
<td>Ethanol Extract (300 mg/kg p.o)</td>
<td>529.67±1.91</td>
<td>129.33±1.43</td>
</tr>
</tbody>
</table>

Values are the mean ± SEM, SEM = standard error of the mean (n = 6), Symbols represent statistical significance.* p < 0.05, ** p < 0.01, as compared to control group.  ns = Not Significant.

CNS DEPRESSANT ACTIVITY

Forced swim test

The possible CNS depressant effect of ethanol extracts of *M. paradisiaca* cv. Puttabale after oral administration was studied by the forced swimming test. Animals treated with the extracts (100 mg, 200 mg and 300 mg/kg) showed decrease in their immobility times, which was significant (151.00±1.98, 106.33±1.80 and 59.50±1.34, respectively). When compared with the control group (179.67±1.09). Similarly, animals treated with the standard drug imipramine (10 mg/kg), as expected showed a significant decrease in their immobility time (40.33±1.28).
Muscle co-ordination test

The ethanol extracts of *M. paradisiaca* cv. Puttabale showed significant effect on the motor coordination as determined by the rotarod performance, which revealed a significant decrease in the spontaneous motor activity in mice. This effect was observed after 1h of drug administration. Results of motor coordination test revealed that the ethanol extract exhibited noticeable reduction in motor coordination in mice after an oral administration. Significant effect was observed at dose of 300 mg/kg (89.32%) than 200 mg (64.88%) and 100 mg (32.12%). On the other hand, the chlorpromazine hydrochloride treated group revealed a statistically significant decrease in motor coordination activity (94.93%) as compared with the control (2.05%) this negligible percentage observed in the control group (Table 5).

**Table 5: CNS Activity using Muscle coordination test by Rotarod**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Treatment</th>
<th>Mean reaction time before drug administration (sec)</th>
<th>Mean reaction time after drug administration (sec)</th>
<th>% Decrease in time</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Normal Control</td>
<td>577.17±1.19</td>
<td>565.33±1.26</td>
<td>2.05</td>
</tr>
<tr>
<td>II</td>
<td>2% DMSO Standard Drug Imipramine (10 mg/kg)</td>
<td>605.17±1.40**</td>
<td>30.67±1.12**</td>
<td>94.93</td>
</tr>
<tr>
<td>III</td>
<td>Ethanol Extract (100 mg/kg p.o)</td>
<td>593.50±1.12**</td>
<td>402.83±2.34**</td>
<td>32.12</td>
</tr>
<tr>
<td>IV</td>
<td>Ethanol Extract (200 mg/kg p.o)</td>
<td>617.00±1.29**</td>
<td>216.67±2.11**</td>
<td>64.88</td>
</tr>
<tr>
<td>V</td>
<td>Ethanol Extract (300 mg/kg p.o)</td>
<td>602.83±1.80**</td>
<td>64.33±2.16**</td>
<td>89.32</td>
</tr>
</tbody>
</table>

Values are the mean ± SEM, SEM = standard error of the mean (n = 6), Symbols represent statistical significance.* p < 0.05, ** p < 0.01, as compared to control group. ns = Not Significant.

**ANTINOCICEPTIVE ACTIVITY**

Writheing method

The number of writhes observed during 20 min period in control group was 86.17±1.70. The crude extract at the dose of 100 mg, 200 mg and 300 mg/kg reduced the number of writhes to 58.33±1.45 (32.30% protection), 33.17±1.19 (61.50% protection) and 23.67±0.67 (72.53% protection) respectively. These values indicated that the responses were dose dependent. Results also indicated that the corm extract in different concentrations was showed to be less
potent than standard drug acetyl salicylic acid which showed 17.33±1.05 (79.88 % protection) writhes. All the readings found to be significant (p<0.01, when compared to control). The results of acetic acid induced writhing test are depicted (Table 6).

Table 6: Antinociceptive activity by Writhing Method

<table>
<thead>
<tr>
<th>Groups</th>
<th>Drug treatment</th>
<th>Dose</th>
<th>Number of writhes</th>
<th>% inhibition of writhings</th>
</tr>
</thead>
<tbody>
<tr>
<td>I.</td>
<td>Control (acetic acid)</td>
<td>10 ml/kg (i.p.)</td>
<td>86.17± 1.70</td>
<td>_</td>
</tr>
<tr>
<td>II.</td>
<td>Acetyl salicylic acid</td>
<td>100 mg/kg (p.o.)</td>
<td>17.33 ± 1.05 **</td>
<td>79.88</td>
</tr>
<tr>
<td>III.</td>
<td>Ethanol extract</td>
<td>100 mg/kg (p.o.)</td>
<td>58.33± 1.45 **</td>
<td>32.30</td>
</tr>
<tr>
<td>IV.</td>
<td>Ethanol extract</td>
<td>200mg/kg (p.o.)</td>
<td>33.17± 1.19 **</td>
<td>61.50</td>
</tr>
<tr>
<td>V.</td>
<td>Ethanol extract</td>
<td>300 mg/kg (p.o.)</td>
<td>23.67± 0.67 **</td>
<td>72.53</td>
</tr>
</tbody>
</table>

Values are the mean ± SEM, SEM = standard error of the mean (n = 6), Symbols represent statistical significance.* p < 0.05, ** p < 0.01, as compared to control group. ns = Not Significant.

Tail flick method
In tail flick method, throughout the 3h observation, animals pretreated with normal saline did not show significant effect on the latent period of tail-flick response. The antinociceptive effects of corm extract in three different dosages were evident within 1.5 h following oral administration and the effect remained significant (p<0.01) throughout the 3h observation period. Comparatively, 300 mg/kg showed highly significant antinociceptive activity. But the antinociceptive activity was decreased after 1.5 hr. The effects of crude extract on nociceptive responses induced by noxious heat (50 °C) are shown in (Table 7).
Table 7: Antinociceptive activity by Tail Flick Method

<table>
<thead>
<tr>
<th>Group (N)</th>
<th>Dose (p.o) ml/kg</th>
<th>Reaction time in min</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>15 Min</td>
</tr>
<tr>
<td>I. Normal Control (Saline)</td>
<td>10</td>
<td>2.00±</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.26</td>
</tr>
<tr>
<td>II. Acetyl salicylic acid</td>
<td>100</td>
<td>11.33±</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.67**</td>
</tr>
<tr>
<td>III. Ethanol extract</td>
<td>100</td>
<td>6.83±</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.48**</td>
</tr>
<tr>
<td>IV. Ethanol extract</td>
<td>200</td>
<td>8.67±</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.33**</td>
</tr>
<tr>
<td>V. Ethanol extract</td>
<td>300</td>
<td>10.67±</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.49**</td>
</tr>
</tbody>
</table>

Values are the mean ± SEM, SEM = standard error of the mean (n = 6), Symbols represent statistical significance.

*p < 0.05, **p < 0.01, as compared to control group. ns = Not Significant.

Hot plate method

The ethanolic extracts of *M. paradisiaca* administrated intraperitoneally in a dose of 100, 200 and 300 mg/kg in mice has shown significant analgesic activity in hot plate method as supported by increase in reaction time at 15 min, 30 min, 45 min, 60 min, 90 min, 120 min, 150 min and 180 min intervals (P<0.01). The increase in reaction time is dose dependent. Maximum analgesic effect was observed at 120 min interval (Table 8).
### Table 8: Antinociceptive activity by Hot Plate Method

<table>
<thead>
<tr>
<th>Group (N)</th>
<th>Dose (p.o) mg/kg</th>
<th>Reaction time in min</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>15 Min</td>
</tr>
<tr>
<td>I. Normal Control (Saline)</td>
<td>10</td>
<td>2.17±</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.31</td>
</tr>
<tr>
<td>II. Acetyl salicylic acid</td>
<td>100</td>
<td>5.67±</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.33**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.83±</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.31*</td>
</tr>
<tr>
<td>III. Ethanol extract</td>
<td>100</td>
<td>3.50±</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.43*</td>
</tr>
<tr>
<td>IV. Ethanol extract</td>
<td>200</td>
<td>4.50±</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.43**</td>
</tr>
</tbody>
</table>

Values are the mean ± SEM, SEM = standard error of the mean (n = 6), Symbols represent statistical significance.* p < 0.05, ** p < 0.01, as compared to control group. ns = Not Significant.
DISCUSSION

In MES-induced convulsion, the *M. paradisiaca* extract significantly protected the animals against seizures by increased the onset and reduced the duration of seizures. The existing antiepileptic drugs (AEDs) that are clinically effective in managing the generalized tonic–clonic and partial seizures such as carbamazepine, phenytoin, primidone, phenobarbital, valproate and lamotrigine all suppress hind limb tonic extension (HLTE) in MES\(^{[58]}\). The ability of the corm ethanol extract to inhibit the HLTE in MES as compared to phenytoin (100% protection) in the model suggests anticonvulsant activity for generalized tonic–clonic and partial seizures. PTZ-induced seizures are similar to the symptoms observed in the absence seizures and drugs such as valproate and ethosuximide which are useful in the management of absence seizures inhibit PTZ-induced seizures\(^{[59]}\). At cellular level, one of the basic mechanisms of actions of anti-epileptic drugs (AEDs) such as ethosuximide and valproate is the suppression of T-type calcium currents in thalamic neurons \(^{[60,61]}\). The extract of *M. paradisiaca* had increased the latency and the incidence of seizures as compared to diazepam. This extract might be useful in the management of seizures by possible interaction between constituents of the crude extract. The majority of currently available antiepileptic drugs fall into one of two pharmacological classes, those that modulate neuronal voltage-gated sodium channels (e.g. carbamazepine, phenytoin, lamotrigine, and topiramate) and those that modulate inhibitory GABAergic neurotransmission (e.g. benzodiazepine, vigabatrin and tiagabine). The ability of the extract may exhibit activity against these two types of seizures and may act through different mechanisms to elicit its anticonvulsant effects, such as voltage-gated sodium, calcium, and potassium or GABAergic pathway. The results of the study have demonstrated that *M. paradisiaca* possessed anticonvulsant activity on the animal models.

The injection of acetic acid is reported to induce the release of mediators of pain such as serotonin, bradykinin, histamine, prostaglandins and other cyclokinase\(^{[62,63]}\). In present study, corm extracts of *M. paradisiaca* showed significant antinoceptive activity. There may be more possible for inhibiting the actions of cyclooxygenase, the enzyme responsible for producing prostaglandins from arachidonic acids. In the central analgesic test, pain threshold of mice towards heat significantly increased the reaction time in both tail-flick and hot plate methods implying its central analgesic activity in dose depended manner. Analgesic activities have earlier been observed in glycosides, tannins and flavonoids compounds\(^{[64,65]}\). Since, leaves aqueous extract of *Musa paradisiaca* showed analgesic activity\(^{[66]}\). Many of the
investigators have evaluated the antinociceptive property of various herbal extracts using experimental mice[67,68]. The significant effect of the phytoextracts is due to the presence of a single active constituent in higher levels or due to the combined effect of more than one phytoconstituent.

CONCLUSION
The qualitative and quantitative analyses of corm ethanol extract of M. paradisiaca cv. Puttabale showed presence of abundant phenolic acids and flavonoids compound might play a significant role in anticonvulsant, CNS depressant and antinociceptive activity against different in vivo models. Fractionation and characterization of bioactive constituent from crude extract will be the future work to investigate.

ACKNOWLEDGEMENTS
The authors are grateful to the Registrar Kuvempu University and the Chairman, Department of Biotechnology and Bioinformatics, Kuvempu University for accessing the laboratory assistance and providing necessary facilities.

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