

4. RESULTS

4.1 - ANXIOLYTIC STUDIES (Acute)

4.1.1- *Trigonella foenum-graecum*

(ME- Methanolic extract of fenugreek seeds; EAF- Ethylacetate fraction of methanolic extract; vehicle- distilled water)

4.1.1.1- Elevated plus maze

The vehicle treated mice spent 31.77 ± 6.23 sec in the open arms. They showed 2.55 ± 0.55 sec and 5.55 ± 1.7 sec as entries in the open and closed arms respectively, whereas animals treated with ME (100 mg/kg), EAF (30 mg/kg) and EAF (100 mg/kg) significantly ($P < 0.05$) spent 74.4 ± 14.51 sec, 83.4 ± 16.39 sec and 99.0 ± 9.53 sec respectively in the open arms. EAF (100 mg/kg) also significantly ($P < 0.05$) increased the entries in the open arms (9.0 ± 1.05) and closed arms (11.75 ± 1.5) (Table 10).

4.1.1.2- Light/Dark test

The vehicle treated group spent 60.89 ± 10.05 sec in the lit box and showed 7.22 ± 0.74 as number of transitions, whereas animals treated with EAF (30 mg/kg) showed a significant ($P < 0.05$) increase in the time spent in lit box (134.6 ± 28.41 sec) (Table 11).

4.1.1.3- Open field apparatus test

The vehicle treated mice showed 2.28 ± 0.68 rearing, 26.71 ± 2.75 assisted rearings and 111.57 ± 5.14 squares traversed during the test interval of 5 min. The EAF (30 mg/kg) significantly ($P < 0.05$) increased the number of rearings as 29.0 ± 3.48 . EAF (100mg/kg) significantly ($P < 0.05$) increased the assisted rearings to 36.75 ± 3.96 and the number of squares traversed to 149.75 ± 17.49 (Table 12).

4.1.2- *Zingiber officinale*

(PE-Pet ether extract of ginger rhizome; TF-Toluene fraction of PE; vehicle- distilled water containing Tween 80 whose volume does not exceed 0.05% of the total volume)

4.1.2.1-Elevated plus maze

The vehicle treated mice spent 41.29 ± 6.29 sec in the open arms and showed 2.8 ± 0.86 entries in the open arms, whereas, animals treated with PE (30 mg/kg) and TF (30 mg/kg) significantly ($P < 0.05$) spent 117.5 ± 12.29 sec and 112.0 ± 9.22 sec respectively in the open arms. PE (30 mg/kg) and TF (30 mg/kg) also significantly ($P < 0.05$) increased the number of entries in the open arms as 6.6 ± 1.07 and 8.0 ± 1.23 respectively (Table 13).

4.1.2.2-Light/Dark test

The vehicle treated group spent 81.0 ± 11.48 sec in the lit box and showed 7.22 ± 0.74 number of transitions, whereas animals treated with PE (100 mg/kg) spent significantly ($P < 0.05$) 125.6 ± 12.48 sec in the lit box. Both PE (30 mg/kg) and TF (30 mg/kg) significantly ($P < 0.05$) increased the number of transitions as 17.6 ± 2.35 and 16.67 ± 1.84 respectively (Table 14).

4.1.2.3-Open field apparatus test

The vehicle treated mice traversed 102.6 ± 5.48 squares and reared 19.2 ± 2.67 times during the observation interval of 5 min. PE (10 and 30 mg/kg) and TF (10 and 30 mg/kg) significantly ($P < 0.05$) increased the number of squares traversed as 170.0 ± 20.25 , 186.4 ± 13.38 and 167.0 ± 12.25 , 189.0 ± 11.34 respectively while, TF (30 mg/kg) significantly ($P < 0.05$) increased the rearings to 40.6 ± 3.65 (Table 15).

4.1.3 -*Panax pseudoginseng* and *Korean ginseng*

(PPE- n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes; KGE- Ethanol extract of *Korean ginseng* roots; vehicle-distilled water)

In all the studies reported below, we have compared the effects of Indian variety of ginseng- *Panax pseudoginseng* extract with a typical known anxiolytic of its own family – *Korean ginseng*.

4.1.3.1-Elevated plus maze

The vehicle treated mice spent 22.8 ± 6.44 sec in the open arm and showed 2.8 ± 0.86 entries in open arm, whereas animals treated with PPE (10 mg/kg) and KGE (10 mg/kg) significantly ($P < 0.05$) spent 82.0 ± 10 sec and 87.0 ± 15.91 sec respectively in the open arm. PPE (10 mg/kg) and KGE (10 mg/kg) also significantly ($P < 0.05$) increased the entries in the open arms as 6.4 ± 0.24 and 6.6 ± 1.07 respectively (Table 16).

4.1.3.2-Light/Dark test

The vehicle treated group spent 81.0 ± 11.48 sec in the lit box and showed 7.22 ± 0.74 as number of transitions, whereas animals treated with PPE (10 mg/kg) and KGE (10 mg/kg) showed a significant ($P < 0.05$) increase in the number of transitions as 19.0 ± 0.89 and 17.6 ± 2.35 respectively (Table 17).

4.1.3.3-Open field apparatus test

The vehicle treated mice traversed 102.6 ± 5.48 squares and showed 19.2 ± 2.67 rearings during the observation interval of 5 min. PPE (3 and 10 mg/kg) and KGE (3 and 10 mg/kg) significantly ($P < 0.05$) increased the number of squares traversed as 171.4 ± 11.03 , 182.4 ± 12.18 and 180 ± 20.25 , 186.4 ± 13.38 respectively. PPE (10 mg/kg) and KGE (10 mg/kg) significantly ($P < 0.05$) increased the rearings as 37.4 ± 1.69 and 40.6 ± 3.65 respectively (Table 18).

4.1.3.4-Hole board apparatus

The vehicle treated mice showed 24.2 ± 4.69 head dips. PPE (3 and 10 mg/kg) and KGE (3 and 10 mg/kg) significantly ($P < 0.05$) increased the number of head dips as 45 ± 1.14 , 48.6 ± 2.20 and 47.6 ± 5.24 , 52 ± 6.18 respectively (Table 19).

4.2-ANXIOLYTIC STUDIES (Chronic)

4.2.1-Trigonella foenum- graecum

(ME-Methanolic extract of fenugreek seeds; EAF-Ethylacetate fraction of methanolic extract; MF- Methanolic fraction of methanolic extract; vehicle- distilled water)

4.2.1.1-Elevated T- maze

Treatment with Ketanserin (0.1 mg/kg) impaired inhibitory avoidance performance in the Elevated T maze. One -way ANOVA showed a non- significant effect of treatment [$F(7,32)=1.91$] and [$F(7,32)=2.11$] for Avoidance-1 and Avoidance-2 respectively. The Dunnett's test showed that none of the treatments significantly increased the latency to leave the enclosed arm as compared to vehicle and other treatment groups. Ketanserin (0.1mg/kg) did not impair the escape latency for all the trials as compared to control. Treatment with ME, EAF and MF did not facilitate escape latency. One -way ANOVA showed an insignificant effect of treatment [$F(7,32)=1.04$] and [$F(7,32)=0.91$] for Escape-1 and Escape-2 respectively (Table 20).

4.2.1.2-Open field apparatus test

Ketanserin (0.1 mg/kg) facilitated locomotion as compared to vehicle and other treatment groups [$F(7,32)=6.26$; $P < 0.05$]. However treatment with ME, EAF and MF groups did not significantly change the squares traversed (Table 21).

4.2.2-Zingiber officinale

(PE-Pet ether extract of ginger rhizome; TF-Toluene fraction of PE; vehicle- distilled water containing Tween 80 whose volume does not exceed 0.05% of the total volume)

4.2.2.1-Elevated T-maze

PE and TF impaired inhibitory avoidance and did not facilitate the escape latency. Treatment with Ondansetron (1mg/kg) significantly impaired inhibitory avoidance performance in the Elevated T maze. One -way ANOVA showed a significant effect of treatment [F (6,28)=34.64; P<0.05] and [F (6,28)=11.63; P<0.05] for Avoidance-1 and Avoidance-2 respectively. The Dunnett's test showed that PE (100mg/kg), TF (10 mg/kg) and TF (30 mg/kg) significantly (P<0.05) increased the latency to leave the enclosed arm (P<0.05) as compared to vehicle and other treatment groups. Ondansetron (1mg/kg) did not impair the escape latency for all the trials as compared to control. One -way ANOVA showed a significant effect of treatment [F (6,28)=5.56; P<0.05] and [F (6,28)=3.74] for Escape-1 and Escape-2 respectively. The Dunnett's test showed that PE (100mg/kg) significantly increased the latency to leave the open arm (P<0.05) as compared to vehicle treated group (Table 22).

4.2.2.2-Open field apparatus test

Ondansetron significantly facilitated locomotion as compared to vehicle or PE and TF treatment groups [F (6,28)=2.77; P<0.05] (Table 23).

4.2.3- *Panax pseudoginseng* and *Korean ginseng*

(PPE- n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes; KGE- Ethanol extract of *Korean ginseng* roots; vehicle-distilled water)

In all the studies reported below, we have compared the effects of Indian variety of ginseng- *Panax pseudoginseng* extract with a typical known anxiolytic of its own family – *Korean ginseng*.

4.2.3.1-Elevated T-maze

Panax pseudoginseng and *Korean ginseng* extract significantly ($P < 0.05$) impaired inhibitory avoidance and did not facilitate escape latency. Treatment with diazepam (1mg/kg) impaired inhibitory avoidance performance in the Elevated T maze. One –way ANOVA showed a significant effect of treatment [$F(7,32) = 25.86$; $P < 0.05$] and [$F(7,32) = 14.75$; $P < 0.05$] for Avoidance-1 and Avoidance-2 respectively. The Dunnett's test showed that PPE (10, 30 and 100 mg/kg) and KGE (10, 30 and 100 mg/kg) decreased the latency to leave the enclosed arm ($P < 0.05$) as compared to vehicle. Diazepam (1mg/kg) did not impair the escape latency for all the trials as compared to control. One –way ANOVA showed a non-significant effect of PPE and KGE treatment [$F(7,32) = 0.86$] and [$F(7,32) = 1.32$] for Escape-1 and Escape-2 respectively (Table 24).

4.2.3.2-Open field apparatus test

Diazepam facilitated locomotion as compared to vehicle, PPE and KGE treatment groups. PPE and KGE at any of the selected dose did not impair locomotion [$F(7,32) = 4.68$; $P < 0.05$] (Table 25).

4.3-OTHER TESTS

ME - Methanolic extract of fenugreek seeds

EAF- Ethylacetate fraction of methanolic extract of fenugreek seeds

PE- Pet ether extract of ginger rhizome

TF-Toluene fraction of PE of ginger rhizome

PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes

KGE - Ethanolic extract of *Korean ginseng* roots

4.3.1-Behavioral assessment

Mice treated with ME (100 mg/kg), EAF (30 mg/kg), PE (50 mg/kg), TF (30 mg/kg), PPE (50 mg/kg) and KGE (50 mg/kg) did not exhibit any abnormal signs. In the initial phase, body position, locomotion, rearing, respiration were normal. There were no tremors or abnormal gait. The grip strength, pain response and righting reflex were also not affected.

4.3.2-Neurotoxicity test

Mice treated with ME (100 mg/kg), EAF (30 mg/kg), PE (50 mg/kg), TF (30 mg/kg), PPE (50 mg/kg) and KGE (50 mg/kg) were able to maintain equilibrium on the rotating rod for more than 5 min, whereas the animals treated with diazepam exhibited motor in-coordination and the fall off time was significantly ($P<0.05$) reduced to 56 ± 2.81 sec.

4.3.3-Haloperidol induced Catalepsy

In vehicle treated rats, haloperidol produced maximum catalepsy after 120 minutes. The onset of catalepsy was delayed significantly with ME (100 mg/kg), PE (50 mg/kg), PPE (50 mg/kg) and KGE (50 mg/kg) ($P<0.05$) and achieved lower scores as compared to the vehicle control at all times (Table 26).

4.4- ANTIHYPERTENSIVE STUDIES (Acute)

4.4.1-*Trigonella foenum graecum*

(ME- Methanolic extract of fenugreek seeds; MF- Methanolic fraction of methanolic extract of fenugreek seeds; vehicle-distilled water.)

Measurement of blood pressure in rats by invasive (Direct) method

The MBP responses to 5-HT (1–10 µg/kg) and *m*-CPP (0.1mg/kg) were significantly ($P<0.05$) reduced after treatment with ME (30mg/kg), MF (10mg/kg) and Ketanserin (10 µg/kg). However responses to other vasoconstrictive agents were not affected (Fig. 11-14).

4.4.2-*Zingiber officinale*

(PE-Pet ether extract of ginger rhizome; TF-Toluene fraction of PE of ginger rhizome; vehicle- distilled water containing Tween 80 whose volume does not exceed 0.05% of the total volume)

Measurement of blood pressure in rats by invasive (Direct) method

The MBP responses to Adr (1µg/kg), NA (1 µg/kg), PhE (1 µg/kg) and 5-HT (1 µg/kg) were significantly reduced ($P<0.05$) after treatment with PE (10 mg/kg), TF (3 mg/kg) and Ondansetron (1 mg/kg) (Fig.15-17).

4.4.3- *Panax pseudoginseng* and *Korean ginseng*

(PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes; KGE - Ethanolic extract of *Korean ginseng* roots; vehicle-distilled water.)

Measurement of blood pressure in rats by invasive (Direct) method

The MBP responses to Adr (1µg/kg), and 5-HT (1 µg/kg) were significantly reduced ($P<0.05$) after treatment with PPE (3 mg/kg) and KGE (3 mg/kg) (Fig.18, 19).

4. 5- ANTIHYPERTENSIVE STUDIES (Chronic)

4.5.1-*Trigonella foenum graecum*

(ME- Methanolic extract of fenugreek seeds; MF- Methanolic fraction of methanolic extract of fenugreek seeds; vehicle- distilled water)

4.5.1.1-Antihypertensive effect of ME-30 and MF-15 on DOCA-salt hypertensive rats

4.5.1.1.1-Measurement of Blood Pressure by Noninvasive (Indirect) Method

Administration of ME (30mg/kg/day, p.o.) and MF (15 mg/kg/day, p.o.) in DOCA salt unilateral nephrectomised rats significantly ($P<0.05$) reduced the systolic blood pressure at the end of the 3rd week and showed further reduction at the end of the 4th week as compared to DOCA salt hypertensive rats alone, implying an antihypertensive effect of ME and MF of Fenugreek seeds (Fig. 20).

4.5.1.1.2-Effect of ME-30 and MF-15 on vascular reactivity to adrenaline (Adr), noradrenaline (NA) and 5-hydroxytryptamine (5-HT) in DOCA-salt hypertensive rats after completion of 4 week treatment schedule

4.5.1.1.2-Measurement of Blood Pressure by Invasive (Direct) method

Pressor responses to NA, Adr and 5-HT were not significantly altered in case of ME (30mg/kg/day, p.o.) and MF (15 mg/kg/day, p.o.) treated rats as compared to sham control rats. Pressor responses to NA, Adr and 5-HT were significantly ($P<0.05$) increased in case of uninephrectomised DOCA-salt treated hypertensive rats as compared to sham control rats. Pressor responses to 5-HT were significantly ($P<0.05$) reduced in case of uninephrectomised DOCA-salt treated rats, which received ME (30mg/kg/day, p.o.) and MF (15 mg/kg/day, p.o.) for 4 weeks as compared to DOCA-salt hypertensive rats (Fig. 21-23).

4.5.1.2-Antihypertensive effect of ME-100 in fructose induced hypertensive rats

4.5.1.2.1-Measurement of Blood Pressure by Noninvasive (Indirect) Method

Fructose (10% solution) feeding for 6 weeks in rats produced a significant ($P<0.01$) elevation of SBP (177 ± 5.3 mmHg) as compared to control rats (147.6 ± 6.2 mmHg). In control rats, chronic administration of ME (100 mg/kg/day, p.o.) for 6 weeks did not alter SBP (146 ± 3.8 mmHg) as compared to control rats (147.6 ± 6.2 mmHg). However chronic administration of ME (100 mg/kg/day, p.o.) for 6 weeks in fructose fed rats significantly ($P<0.05$) reduced SBP (154.1 ± 5.7 mmHg) as compared to fructose fed hypertensive rats (177 ± 5.3 mmHg) implying an antihypertensive effect (Fig. 24).

4.5.1.2.2- Effect of ME-100 on vascular reactivity to adrenaline, noradrenaline, and 5-hydroxytryptamine in fructose hypertensive rats after completion of 6-week treatment schedule.

4.5.1.2.2-Measurement of Blood Pressure by Invasive (Direct) Method

Pressor responses to NA, Adr and 5-HT were not significantly altered in case of ME-100 treated group as compared to control group. Pressor responses to 5-HT were significantly ($P<0.05$) increased in case of fructose (10%) fed hypertensive rats as compared to control rats. Pressor responses to 5-HT were significantly reduced ($P<0.05$) in rats which received ME-100 fed with fructose (10%) for 6 weeks as compared to fructose (10%) fed hypertensive rats (Fig. 25).

4.5.2-*Zingiber officinale*

(PE-Pet ether extract of ginger rhizome; TF-Toluene fraction of PE of ginger rhizome; vehicle- distilled water containing Tween 80 whose volume does not exceed 0.05% of the total volume)

4.5.2.1-Antihypertensive effect of PE-50 and TF-10 on DOCA-salt hypertensive rats

4.5.2.1.1-Measurement of Blood Pressure by Noninvasive (Indirect) Method

Administration of PE (50 mg/kg/day, p.o.) and TF (10 mg/kg/day, p.o.) in DOCA salt unilateral nephrectomised rats significantly ($P<0.05$) reduced the systolic blood pressure at the end of the 2nd and 3rd week and showed further reduction at the end of the 4th week as compared to DOCA salt hypertensive rats alone, implying an antihypertensive effect of PE and TF (Fig. 26).

4.5.2.1.2-Effect of PE-50 and TF-10 on vascular reactivity to Adr, NA, 5-HT and PBG in DOCA-salt hypertensive rats after 4 weeks of treatment schedule

4.5.2.1.2-Measurement of Blood Pressure by Invasive (Direct) Method

Pressor responses to Adr, NA and 5-HT were not altered significantly in case of PE (50 mg/kg/day, p.o.) and TF (10 mg/kg/day, p.o.) treated rats as compared to sham control rats. Pressor responses to Adr and NA were significantly ($P<0.05$) increased in case of uni-nephrectomised DOCA-salt treated hypertensive rats as compared to sham control rats. Pressor responses to 5-HT was significantly ($P<0.05$) reduced in case of uni-nephrectomised rats which received PE (50 mg/kg/day, p.o.) and TF (10 mg/kg/day, p.o.) compared to sham control and in uni-nephrectomised DOCA-salt treated rats which received PE (50 mg/kg/day, p.o.) and TF (10 mg/kg/day, p.o.) for 4 weeks as compared to DOCA-salt hypertensive rats. Pressor responses to PBG was significantly ($P<0.05$) reduced in case of uni-nephrectomised animals receiving PE (50 mg/kg/day, p.o.) and TF (10 mg/kg/day, p.o.) for 4 weeks as compared to sham control and in uni-nephrectomised DOCA-salt treated rats which received

PE (50 mg/kg/day, p.o.) and TF (10 mg/kg/day, p.o.) for 4 weeks as compared to DOCA-salt hypertensive rats (Fig. 27, 28, 29 and 31).

4.5.2.2-Antihypertensive effect of PE-50 in fructose induced hypertensive rats

4.5.2.2.1-Measurement of Blood Pressure by Noninvasive (Indirect) Method

Fructose (10% solution) feeding for 5 weeks in rats produced a significant ($P<0.05$) elevation of SBP (171.5 ± 6.82 mmHg) as compared to control rats (124.7 ± 3.69 mmHg). However chronic administration of PE (50 mg/kg/day, p.o.) for 5 weeks in fructose fed rats significantly ($P<0.05$) reduced SBP ($132.7.1 \pm 14.03$ mmHg) as compared to fructose fed hypertensive rats (171.5 ± 6.82 mmHg) implying an antihypertensive effect (Fig. 32).

4.5.2.2.2-Effect of PE-50 on vascular reactivity to 5-HT, PBG in fructose hypertensive rats after 5 weeks of treatment schedule

4.5.2.2.2-Measurement of Blood Pressure by Invasive (Direct) Method

Pressor responses to 5-HT were increased significantly ($P<0.05$) in case of fructose (10%) fed hypertensive rats as compared to control rats. Pressor responses to 5-HT were significantly reduced ($P<0.05$) in case of fructose (10%) fed rats, which received PE (50 mg/kg/day, p.o.) for 5 weeks as compared to fructose (10%) fed hypertensive rats. Pressor responses to PBG were significantly reduced ($P<0.05$) in case of fructose (10%) fed rats, which received PE (50 mg/kg/day, p.o.) for 5 weeks as compared to fructose (10%) fed hypertensive rats (Fig. 33, 34).

4.5.3. *Panax pseudoginseng* and Korean ginseng

(PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes;
KGE - Ethanolic extract of *Korean ginseng* roots; vehicle-distilled water.)

In all the studies reported below we have compared the effects of Indian variety of ginseng- *Panax pseudoginseng* extract with a typical known anxiolytic of its own family – *Korean ginseng*.

4.5.3.1-Antihypertensive effect of PPE-30 and KGE-30 in DOCA-salt hypertensive rats

4.5.3.1.1-Measurement of Blood Pressure by Noninvasive (Indirect) Method

Administration of PPE (30 mg/kg/day, p.o.) and KGE (30 mg/kg/day, p.o.) in DOCA salt unilateral nephrectomised rats significantly ($P<0.05$) reduced the systolic blood pressure at the end of the 2nd, 3rd week and showed further reduction at the end of the 4th week as compared to DOCA salt hypertensive rats alone, implying an antihypertensive effect of PPE and KGE (Fig. 36).

4.5.3.1.2-Effect of PPE -30 and KGE-30 on vascular reactivity to Adr, NA and 5-HT in DOCA-salt hypertensive rats after 4 weeks of treatment schedule

4.5.3.1.2- Measurement of Blood Pressure by invasive (direct) Method

Pressor responses to Adr, Nor and 5-HT were not altered significantly in case of PPE (30 mg/kg/day, p.o.) and KGE (30 mg/kg/day, p.o.) treated rats as compared to sham control rats. Pressor responses to Adr, Nor were significantly ($P<0.05$) increased in case of uni-nephrectomised DOCA-salt treated hypertensive rats as compared to sham control rats. Pressor responses to 5-HT was significantly ($P<0.05$) reduced in case of uni-nephrectomised rats which received PPE (30 mg/kg/day, p.o.) and KGE (30 mg/kg/day, p.o.) compared to sham control and in uni-nephrectomised DOCA-salt treated rats which received PPE (30 mg/kg/day, p.o.) and KGE (30 mg/kg/day, p.o.) for 4 weeks as compared to DOCA-salt hypertensive rats (Fig. 27, 28 and 30).

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4.5.3.2-Antihypertensive effect of PPE-30 and KGE-30 in fructose induced hypertensive rats

4.5.3.2.1- Measurement of Blood Pressure by Noninvasive (Indirect) Method

Fructose (10% solution) feeding for 5 weeks in rats produced a significant ($P<0.05$) elevation of SBP (171.5 ± 6.82 mmHg) as compared to control rats (124.7 ± 3.69 mmHg). However chronic administration of PPE (30 mg/kg/day, p.o.) and KGE (30 mg/kg/day, p.o.) for 5 weeks in fructose fed rats significantly ($P<0.05$) reduced SBP (138.5 ± 10.5 mmHg, 132.7 ± 14.03 mmHg) as compared to fructose fed hypertensive rats (171.5 ± 6.82 mmHg) implying an antihypertensive effect (Fig. 32).

4.5.3.2.2- Effect of PPE-30 and KGE-30 on vascular reactivity to 5-HT and ACh in fructose hypertensive rats after completion of 5 weeks treatment schedule.

4.5.3.2.2-Measurement of Blood Pressure by Invasive (Direct) Method

Pressor responses to 5-HT were increased significantly ($P<0.05$) in case of fructose (10%) fed hypertensive rats as compared to control rats. Pressor responses to 5-HT were significantly reduced ($P<0.05$) in case of fructose (10%) fed rats, which received PPE-30 and KGE-30 for 5 weeks as compared to fructose (10%) fed hypertensive rats. Depressor responses to ACh were significantly increased ($P<0.05$) in case of fructose (10%) fed rats, which received PPE-30 and KGE-30 for 5 weeks as compared to fructose (10%) fed hypertensive rats (Fig. 33, 35).

4.6- SOME STUDIES TO SUPPORT THE 5-HT HYPOTHESIS

4.6.1-*Trigonella foenum- graecum*

(ME-Methanolic extract of fenugreek seeds; EAF- Ethylacetate fraction of methanolic extract of fenugreek seeds; MF- Methanolic fraction of methanolic extract)

4.6.1.1-Reversal of *m*-CPP induced anxiety

In EPM, EAF (30, 60, 120, 240, 480 mg/kg) and diazepam (0.5, 1, 2, 4, 8,16 mg/kg) significantly antagonized *m*-CPP (1 mg/kg) in a dose dependent fashion (Table 27).

4.6.1.2-Lithium induced head twitches

In vehicle treated rats, lithium sulphate (200 mg/kg, i.p.) produced 17.4 ± 1.20 head twitches. The administration of ME (100 mg/kg), EAF (30 mg/kg) or MF (30 mg/kg) significantly decreased the number of head twitches to 11.5 ± 2.56 , 6.0 ± 0.70 and 1.0 ± 0.31 respectively (Table 28).

4.6.2-*Zingiber officinale*

(PE-Pet ether extract of ginger rhizome; TF-Toluene fraction of PE of ginger rhizome)

4.6.2.1-GC-MS

The GC-MS of TF showed presence of [6]-gingerol, [8]-gingerol, [10]-gingerol, [6]-shagoal, [8]- shagoal [10]-shagoal and Zingiberone having molecular weights 294, 332, 360, 276, 306, 332 and 194 respectively. They contributed to 13.31 %, 0.73 %, 0.87 %, 26.39 %, 15.87 %, 0.73 %, and 1.51 % respectively (Maryadele *et al.*, 2001). This indicates that TF contains nearly 15% W/W of gingerol- an active fraction of ginger which possesses 5-HT₃ antagonistic properties (Fig. 40).

4.6.3- *Panax pseudoginseng* and *Korean ginseng*

**(PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes;
KGE - Ethanolic extract of *Korean ginseng* roots)**

4.6.3.1-Lithium induced head twitches

In vehicle treated rats, lithium sulphate (200 mg/kg, i.p.) produced 17.4 ± 1.20 head twitches. The administration of PPE (30mg/kg) and KGE (30 mg/kg) significantly decreased the number of head twitches to 11.0 ± 0.50 and 7.0 ± 0.21 respectively (Table 28).

4.6.3.2-Pentobarbital induced sleep

The mice receiving pentobarbital (40 mg/kg, i.p.) slept for 123 ± 8.20 min whereas animals treated with PPE (30 mg/kg) and KGE (30mg/kg) prolonged the sleeping time to 256 ± 24.62 min and 276 ± 21.20 min (Table 29).

4.6.3.3-LC-MS

The LC-MS of PPE showed the presence of ginsenoside Rb1 and ginsenoside Rb2 having m/z as 1131.8 and 1101.6 respectively. Further m/z 1131.8 showed fragmentation pattern as m/z 789.2 and m/z 364.9 (Lutchtefeld, 2004). This also indicates the presence of ginsenoside occurring as 63.6% relative intensity (Fig. 41).

4.6.4-*In-vitro* tests

4.6.4.1-Effect of ME-100 of fenugreek on CDRC (Cumulative dose response curve) of 5-Hydroxytryptamine on isolated rat stomach fundus strip of control and fructose hypertensive rats

Chronic administration of ME (100mg/kg/day, p.o.) for 6 weeks in fructose hypertensive rats shifted dose response curve of 5-HT significantly ($P < 0.001$) to right with suppression of maxima as compared to dose response curve of fructose hypertensive rats on isolated stomach fundus strip. Chronic administration of ME (100mg/kg/day, p.o.) for 6 weeks in control rats

shifted dose response curve of 5-HT significantly to right with suppression of maxima as compared to dose response curve of control rats on isolated stomach fundus strip (Fig. 37).

4.6.4.2-Effect of PE-50 of ginger on CDRC (Cumulative dose response curve) of 5-HT on isolated rat stomach fundus strip of control and fructose hypertensive rats

Chronic administration of PE (50mg/kg/day, p.o.) for 5 weeks in fructose hypertensive rats shifted dose response curve of 5-HT significantly ($P<0.05$) to right with suppression of maxima as compared to dose response curve of fructose hypertensive rats on isolated stomach fundus strip (Fig. 38).

4.6.4.3-Effect of PPE-30 and KGE-30 of ginseng on CDRC (Cumulative dose response curve) of 5-HT on isolated rat stomach fundus strip of control and fructose hypertensive rats

Chronic administration of PPE (30mg/kg/day, p.o.) and KGE (30mg/kg/day, p.o.) for 5 weeks in fructose hypertensive rats shifted dose response curve of 5-HT significantly ($P<0.05$) to right with suppression of maxima as compared to dose response curve of fructose hypertensive rats on isolated stomach fundus strip (Fig. 38).

4.6.5-Coagulation time

Fructose (10% solution) feeding in rats for 5-6 weeks significantly shortened the mean coagulation time (17.6 ± 2.358 sec) as compared to control rats (32.58 ± 4.124 sec.). Chronic administration of ME (100 mg/kg/day, p.o.), PE (50 mg/kg/day, p.o.), PPE (30 mg/kg/day, p.o.) and KGE (30 mg/kg/day, p.o.) for 6 weeks in fructose fed rats significantly prolonged the mean coagulation time (34.2 ± 2.685 sec, 52 ± 5.34 sec, 120.45 ± 5.78 sec and 123.56 ± 6.35 sec respectively) as compared to fructose fed hypertensive rats (17.6 ± 2.358 sec) (Fig. 39).

Table 10

Effect of ME and EAF of *Trigonella foenum-graecum* seeds on time spent in open arms and entries in open and closed arms in elevated plus maze in mice

S.No	Treatment (Dose: mg/kg)	Parameters		
		Time spent in O.A (sec)	Entries in O. A	Entries in C. A
1	Vehicle	31.77±6.23	2.55±0.55	5.55±1.7
2	Diazepam (1)	83.6±13.42*	4.6±0.18	5.2±0.72
3	ME (30)	46.33±5.10	3.33±0.16	3.67±0.19
4	ME (100)	74.4±14.51*	4.4±1.18	5.0±0.77
5	EAF (30)	83.4±16.39*	5.6±0.79*	5.4±0.9
6	EAF (100)	99.0±9.53*	9.0±1.05*	11.75±1.5*
F (5, 24)		4.78	8.84	6.87

n = 5, Values are mean ± SEM. *P< 0.05 compared to vehicle (ANOVA followed by Dunnett's test). O.A= Open arms, C.A= Closed arms

ME - Methanolic extract of *Trigonella foenum graecum* seeds

EAF- Ethylacetate fraction of methanolic extract of *Trigonella foenum graecum* seeds

Table 11

Effect of ME and EAF of *Trigonella foenum- graecum* seeds on time spent in lit zone and number of transitions in light/dark apparatus in mice

S.No	Treatment (Dose: mg/kg)	Time spent in lit zone (sec)	Number of transitions
1	Vehicle	60.89 ±10.05	7.22 ± 0.74
2	Diazepam (1)	121.8 ±8.06*	9.2 ± 1.04
3	ME (30mg/ kg)	108.33± 4.76	10.0 ± 1.76
4	ME (100mg/kg)	105.6 ±21.09	6.0 ± 0.0
5	EAF (30mg/kg)	134.6 ±28.41*	8.4 ±0.83
6	EAF (100 mg/kg)	116.0 ±16.60	7.25 ±1.31
	F (5, 24)	2.23	1.81 (NS)

n= 5, Values are mean ± SEM. *P< 0.05 compared to vehicle (ANOVA followed by Dunnett's test). NS= Not significant.

ME - Methanolic extract of *Trigonella foenum graecum* seeds

EAF- Ethylacetate fraction of methanolic extract of *Trigonella foenum graecum* seeds

Table 12

Effect of ME and EAF of *Trigonella foenum- graecum* seeds on rearing and locomotion in open field apparatus test in mice

S.No	Treatment (mg/kg)	Rearing	Assisted Rearing	Squares traversed
1	Vehicle	2.28±0.68	26.71±2.75	111.57±5.14
2	Diazepam (1)	2.8±1.23	25.2 ±3.08	160.2±16.23*
3	ME (30)	2.0±0.88	36.33 ±1.01	109.0±11.73
4	ME (100)	1.8±0.99	31.4 ±3.77	112.8±11.08
5	EAF (30)	29.0±3.48*	8.6 ±2.21*	104.6±11.05
6	EAF (100)	7.0±0.90	36.75±3.96*	149.75±17.49*
F (5,24)		41.41	12.30	3.03

n = 5, Values are mean ± SEM. *P< 0.05 compared to vehicle (ANOVA followed by Dunnett's test).

ME - Methanolic extract of *Trigonella foenum graecum* seeds

EAF- Ethylacetate fraction of methanolic extract of *Trigonella foenum graecum* seeds

Table 13

Effect of PE and TF of *Zingiber Officinale* on time spent in open arms and entries in open and closed arms in elevated plus maze in mice

S.No	Treatment (mg/kg)	Parameters		
		Time spent in O.A (sec)	Entries in O.A	Entries in C.A
1	Vehicle	41.29 ± 6.29	2.8 ± 0.86	6.2 ± 0.58
2	Diazepam (1)	108 ± 7.90*	8.33 ± 0.76*	8.16 ± 0.60
3	PE (10)	64.0 ± 9.76	4.4 ± 1.53	9.6 ± 1.86
4	PE (30)	117.5 ± 12.29*	6.6 ± 1.07*	9.6 ± 1.20
5	PE (100)	67.83 ± 5.35	2.8 ± 0.2	6.6 ± 0.65
6	TF (10)	74.33 ± 8.54	5.67 ± 1.23	6.9 ± 1.22
7	TF (30)	112.0 ± 9.22*	8 ± 1.23*	9.6 ± 1.20
F (6,28)		11.04	4.64	1.83

n = 5, Values are mean ± SEM. *P < 0.05, as compared to vehicle (ANOVA followed by Dunnett's test). O.A= Open arms, C.A= Closed arms

PE- Pet ether extract of *Zingiber Officinale* rhizomes

TF- Toluene fraction of pet ether extract of *Zingiber Officinale* rhizomes

Observation: An inverse "U" dose response curve [∩] seen in time spent in open arm parameter with increasing doses of PE.

Table 14

Effect of PE and TF of *Zingiber officinale* on time spent in lit zone and number of transitions in light/dark apparatus in mice

S.No	Treatment (mg/kg)	Time spent in lit zone (sec)	Number of transitions
1	Vehicle	81.0 ± 11.48	7.22 ± 0.74
2	Diazepam (1)	121.7 ± 7.95*	14.2 ± 1.39*
3	PE (10)	63.0 ± 9.07	12.8 ± 3.07
4	PE (30)	98.2 ± 7.27	17.6 ± 2.35*
5	PE (100)	125.6 ± 12.48*	12.2 ± 1.02
6	TF (10)	105.4 ± 5.68	14.2 ± 1.63
7	TF (30)	116.8 ± 14.8	16.67 ± 1.84*
F (6,28)		5.76	3.31

n = 5. Values are mean ± SEM. *P < 0.05 as compared to vehicle (ANOVA followed by Dunnett's test).

PE- Pet ether extract of *Zingiber Officinale* rhizomes

TF- Toluene fraction of pet ether extract of *Zingiber Officinale* rhizomes

Table 15

Effect of PE and TF of *Zingiber officinale* on rearing and locomotion in open field apparatus test in mice

S.No	Treatment (mg/kg)	Squares traversed	Rearings
1	Vehicle	102.6±5.48	19.2 ± 2.67
2	Diazepam (1)	173.6±18.73*	23.6 ± 4.94
3	PE (10)	170.0 ±20.25*	16.8 ± 3.83
4	PE (30)	186.4±13.38*	22.12 ± 2.25
5	PE (100)	155.6± 11.79	28.6 ± 1.8
6	TF (10)	167.0 ± 12.25*	35.25 ± 6.35
7	TF (30)	189.0 ± 11.34*	40.6±3.65*
F (6,28)		4.29	4.91

n = 5. Values are mean ± SEM. *P< 0.05, as compared to vehicle (ANOVA followed by Dunnett's test).

PE- Pet ether extract of *Zingiber Officinale* rhizomes

TF- Toluene fraction of pet ether extract of *Zingiber Officinale* rhizomes

Observation: An inverse "U" dose response curve [∩] seen in time spent in open arm parameter with increasing doses of PE.

Table 16

Effect of PPE and KGE on time spent in open arms and entries in open and closed arms in elevated plus maze in mice

S.No	Treatment (mg/kg)	Parameters		
		Time spent in O.A (sec)	Entries in O.A	Entries in C.A
1	Vehicle	22.8±6.44	2.8±0.86	6.2± 0.58
2	Diazepam (1)	78.0 ± 7.90*	8.33±0.76*	8.16±0.60
3	PPE (3)	35.4±0.93	3.6±0.4	8.4±0.4
4	PPE (10)	82.0±10.0*	6.4±0.24*	9.4±0.4
5	PPE (30)	28.8±1.02	1.8±0.37	7±0.31
6	KGE (3)	38.4±9.76	4.4±1.53	9.6±1.86
7	KGE (10)	87.0±15.91*	6.6±1.07*	9.6±1.20
8	KGE (30)	34.0±5.35	2.8±0.2	6.6±0.65
F (7,32)		9.74	8.03	2.37 (NS)

n = 5, Values are mean ± SEM.*P< 0.05, as compared to vehicle (ANOVA followed by Dunnett's test) O.A = Open arms, C.A = Closed arms, NS= Not significant

PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes

KGE - Ethanolic extract of *Korean ginseng* roots.

Observation: An inverse "U" dose response curve [∩] seen in time spent in open arm and entries in open arm parameter with increasing doses of PPE and KGE.

Table 17

Effect of PPE and KGE on time spent in lit zone and number of transitions in light/dark apparatus in mice

S.No	Treatment (mg/kg)	Time spent in lit zone (sec)	Number of transitions
1	Vehicle	81.0 ± 11.48	7.22 ± 0.74
2	Diazepam (1)	121.7 ± 7.95*	162 ± 1.39*
3	PPE (3)	58.2 ± 4.16	10 ± 0.70
4	PPE (10)	86.8 ± 3.81	19 ± 0.89*
5	PPE (30)	69.8 ± 11.65	9.8 ± 0.73
6	KGE (3)	60.0 ± 16.07	12.8 ± 3.07
7	KGE (10)	94.2 ± 7.27	17.6 ± 2.35*
8	KGE (30)	75.6 ± 12.48	12.2 ± 1.02
F (7,32)		4.11	6.80

n = 5. Values are mean ± SEM. *P < 0.05, as compared to vehicle (ANOVA followed by Dunnett's test).

PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes

KGE - Ethanolic extract of *Korean ginseng* roots

Observation: An inverse "U" dose response curve [∩] seen in time spent in lit zone and number of transition parameters with increasing doses of PPE and KGE.

Table 18

Effect of PPE and KGE on rearing and locomotion in open field apparatus test in mice

S.No	Treatment (mg/kg)	Squares traversed	Rearings
1	Vehicle	102.6±5.48	19.2± 2.67
2	Diazepam (1)	173.6±18.73*	36.6±4.94*
3	PPE (3)	171.4±11.03*	23.8±0.73
4	PPE (10)	182.4±12.18*	37.4±1.69*
5	PPE (30)	126±8.30	22.2±2.39
6	KGE (3)	180.0 ±20.25*	26.8±3.83
7	KGE (10)	186.4±13.38*	40.6±3.65*
8	KGE (30)	135.6± 11.79	28.6±1.8
F (7,32)		5.45	6.93

n = 5. Values are mean ± SEM. *P< 0.05, as compared to vehicle (ANOVA followed by Dunnett's test).

PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes

KGE - Ethanolic extract of *Korean ginseng* roots

Observation: An inverse "U" dose response curve [∩] seen in number of squares traversed and rearing parameters with increasing doses of PPE and KGE.

Table 19

Effect of PPE and KGE on number of head poking in hole board apparatus in mice

S.No	Treatment (mg/kg)	No. of head poking
1	Vehicle	24.2±4.69
2	Diazepam (1)	44.8±2.08*
3	PPE (3)	45±1.14*
4	PPE (10)	48.6±2.20*
5	PPE (30)	26.6±1.4
6	KGE (3)	47.6±5.24*
7	KGE (10)	52±6.18*
8	KGE (30)	31.4± 6.90
F (7,32)		6.40

n = 5. Values are mean ± SEM. *P< 0.05, as compared to vehicle (ANOVA followed by Dunnett's test).

PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes

KGE - Ethanolic extract of *Korean ginseng* roots

Observation: An inverse "U" dose response curve [∩] seen in number of head pokes parameter with increasing doses of PPE and KGE.

Table 20

Effect of ME, EAF and MF of *Trigonella foenum- graecum* on inhibitory avoidance and escape latency in elevated T-maze in mice

S. No	Treatment (mg/kg)	Inhibitory Avoidance (sec)		Escape latency (sec)	
		Avoidance-1	Avoidance-2	Escape-1	Escape-2
1	Vehicle	11.57±3.38	10.43±3.53	20.29±8.70	28.43±13.43
2	Ketanserin (0.1)	4.33±0.80	8.83±1.51	29.33±13.91	28.67±13.67
3	ME (30)	8.0±1.63	6.83±1.47	10.17±2.19	15.5±3.38
4	ME (100)	10.0±0.85	8.5±1.11	44.5±27.25	82.5±43.93
5	EAF (10)	9.0±1.71	9.66±2.92	19.83±4.84	29.67±9.91
6	EAF (30)	8.0±1.46	11.83±3.54	12.17±2.30	11.33±4.55
7	MF (10)	11.83±2.49	18.17±3.41	16.83±4.98	20.83±5.65
8	MF (30)	6.5±0.341	6.83±0.40	12.17±2.10	16.17±3.75
	F (7, 32)	1.91 (NS)	2.11 (NS)	1.04 (NS)	0.91 (NS)

n = 5, values are mean ± SEM. *P< 0.05, as compared with vehicle (ANOVA followed by Dunnett's test). NS= Not significant

ME - Methanolic extract of fenugreek seeds

EAF- Ethyl acetate fraction of methanolic extract of *Trigonella foenum graecum* seeds

MF – Methanol fraction of methanolic extract of *Trigonella foenum graecum* seeds

Table 21

Effect of ME, EAF and MF of *Trigonella foenum- graecum* on number of squares traversed in open field apparatus test in mice

S.No	Treatment (mg/kg)	Squares traversed
1	Vehicle	96.71±4.01
2	Ketanserin (0.1)	135.0±8.59*
3	ME (30)	102.2±5.95
4	ME (100)	65.0±9.68
5	EAF (10)	103.3±4.91
6	EAF (30)	103.3±9.26
7	MF (10)	77.5±7.25
8	MF (30)	92.0±12.72
	F (7, 32)	6.26

n = 5, values are mean ± SEM. *P< 0.05, as compared to vehicle (ANOVA followed by Dunnett's test).

ME - Methanolic extract of fenugreek seeds

EAF- Ethyl acetate fraction of methanolic extract of *Trigonella foenum graecum* seeds

MF – Methanol fraction of methanolic extract of *Trigonella foenum graecum* seeds

Table 22

Effect of PE and TF of *Zingiber officinale* on inhibitory avoidance and escape latency in elevated T- maze in mice

S. No	Treatment (mg/kg)	Inhibitory Avoidance (sec)		Escape latency (sec)	
		Avoidance-1	Avoidance-2	Escape-1	Escape-2
1	Vehicle	16±1.34	65.2±11.99	24±7.02	71.0±12.03
2	Ondansetron (1)	5.6±0.4*	17.4±4.75*	61.0±10.33*	89.8±15.79
3	PE (10)	17.6±0.81	51.8±10.79	25.4±5.06	46.4±13.54
4	PE (30)	9.0±0.54*	108.0±20.83	38.4±7.27	84.0±16.55
5	PE (100)	6.6±0.50*	20.0±4.23*	72.0±13.78*	100.0±12.14
6	TF (10)	9.8±1.24*	17.6±1.50*	59.6±9.59	164.6±36.77
7	TF (30)	5.8±0.37*	15.2±2.15*	23.8±2.81	85.8±111.49
	F (6,28)	34.64	11.63	5.56	3.74 (NS)

n = 5, values are mean ± SEM. *P< 0.05, as compared to vehicle (ANOVA followed by Dunnett's test). NS= Not significant

PE- Pet ether extract of *Zingiber Officinale* rhizomes

TF- Toluene fraction of pet ether extract of *Zingiber Officinale* rhizomes

Table 23

Effect of PE and TF of *Zingiber officinale* on locomotion in open field apparatus test in mice

S.No	Treatment (mg/kg)	Squares traversed
1	Vehicle	75.8±14.54
2	Ondansetron (1)	121.4± 8.21*
3	PE (10)	108.2±16.71
4	PE (30)	88.0± 6.05
5	PE (100)	88.0±10.91
6	TF (10)	107.6±3.35
7	TF (30)	73.0±10.38
F (6,28)		2.77

n = 5, Values are mean ± SEM. *P< 0.05, as compared to vehicle (ANOVA followed by Dunnett's test).

PE- Pet ether extract of *Zingiber Officinale* rhizomes

TF- Toluene fraction of pet ether extract of *Zingiber Officinale* rhizomes

Table 24

Effect of PPE and KGE on inhibitory avoidance and escape latency in elevated T-maze in mice

S. No	Treatment (mg/kg)	Inhibitory Avoidance (sec)		Escape latency (sec)	
		Avoidance-1	Avoidance-2	Escape-1	Escape-2
1	Vehicle	16.0±1.34	65.2±11.99	24.0±7.02	51.0±12.03
2	Diazepam (1)	4.33±0.80*	8.83±1.51*	29.33±13.91	28.61±13.67
3	PPE (10)	8.2±0.37*	19.2±0.86*	21.2±1.39	24.0±0.70
4	PPE (30)	6.6±0.4*	12.4±0.92*	13.6±3.07	23.6±1.20
5	PPE (100)	3.4±0.50*	7.4±0.50*	13.0±4.26	24.8±3.39
6	KGE (10)	9.2±0.66*	24.2±3.23*	26.6±6.11	26.8±5.18
7	KGE (30)	6.8±1.2*	15.4±6.08*	16.4±4.35	28.4±4.46
8	KGE (100)	3.4±0.67*	9.2±1.5*	16.4±4.61	28.6±9.6
	F (7,32)	25.86	14.75	0.86 (NS)	1.32 (NS)

n = 5, values are mean ± SEM. *P < 0.05, as compared to vehicle (ANOVA followed by Dunnett's test). NS = Not significant

PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes

KGE - Ethanolic extract of *Korean ginseng* roots

Table 25

Effect of PPE and KGE on locomotion in open field apparatus test in mice

S.No	Treatment (mg/kg)	Squares traversed
1	Vehicle	75.8±14.54
2	Diazepam (1)	121.0±8.59*
3	PPE (10)	55.6±13.93
4	PPE (30)	66.6±2.61
5	PPE (100)	55.0±4.58
6	KGE (10)	65.4±12.69
7	KGE (30)	70.4±8.68
8	KGE (100)	61.6±5.16
	F (7,32)	4.68

n = 5, values are mean ± SEM. *P < 0.05, as compared to vehicle ANOVA followed by Dunnett's test.

PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes

KGE - Ethanolic extract of *Korean ginseng* roots

Table 26

Effect of ME, PE, PPE and KGE on haloperidol (3 mg/kg, i.p) induced catalepsy in rats

Time (min)	Vehicle	ME (100mg/kg)	PE (50mg/kg)	PPE (50mg/kg)	KGE (50mg/kg)
0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0
15	0.5 ± 0	0 ± 0	0.5 ± 0	0 ± 0	0 ± 0
30	1.1 ± 0.24	0.33 ± 0.16	0.5 ± 0	0.2 ± 0.12*	0.2 ± 0.12*
60	2.3 ± 0.73	0.33 ± .16	1.1 ± 0.24	0.2 ± 0.12*	0.2 ± 0.12*
90	2.7 ± 0.48	0.50 ± 0.0*	1.5 ± 0.0	0.2 ± 0.12*	0.2 ± 0.12*
120	3.16 ± .33	1.16 ± .33	0.5 ± 0.0*	0.2 ± 0.12*	0.2 ± 0.12*

n = 5, Values are mean ± SEM. *P < 0.05, as compared to vehicle (Kruskal Wallis test followed by Dunn's multiple comparison test).

ME - Methanolic extract of fenugreek seeds

PE- Pet ether extract of *Zingiber Officinale* rhizomes

PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes

KGE - Ethanolic extract of *Korean ginseng* roots

Table 27

Reversal of *m*-CPP by EAF and Diazepam on time spent in open arms and entries in open and closed arms in elevated plus maze in mice

S. No	Treatment (Dose: mg/kg)	Time spent in O.A	Entries in O.A	Entries in C.A	Head dips
1	Vehicle	31.77±6.23	2.55±0.55	5.55±1.7	6±2.30
2	<i>m</i> -CPP(1)	10.25±5.04*	1.75±0.75	3.75±0.94	2.75±2.13*
3	<i>m</i> -CPP +EAF(30)	23.25±3.32	2.35±0.47	5.25±0.85	2.5±0.27*
4	<i>m</i> -CPP +EAF(60)	36.5±12.23	3.0±0.57	9.5±1.5*	7.5±5.48
5	<i>m</i> -CPP +EAF(120)	73.25 ±23.44	4.5±0.64	7.25±0.7	9.0±5.03
6	<i>m</i> -CPP +EAF(240)	79.0±16.02*	2.16±0.57	5.0±0.5	19.0±0.5*
7	<i>m</i> -CPP +EAF(480)	61.0±15.25	3.5±1.25	4.0±1.35	9.5±1.04
8	EAF(60)	147.16±40.11*	6.0±2.29*	4.7±1.15	9.0±3.28
9	Diazepam(1.5)	95.0±13.64*	5.5±0.28	8.75±0.6*	13.0±1.22
10	<i>m</i> -CPP + Diazepam(0.5)	22.25±8.32	2.5±0.95	7.5±0.64	2.25±0.25
11	<i>m</i> -CPP + Diazepam (1)	21.75±4.80	2.25±0.47	4.25±0.85	0.75±0.47
12	<i>m</i> -CPP + Diazepam (2)	36.75±4.80	1.75±0.47	6.0±1.41	2.75±0.47
13	<i>m</i> -CPP + Diazepam (4)	63.75±18.15	4.75±2.92	5.25±2.65	10.5±5.35
14	<i>m</i> -CPP + Diazepam (8)	147.0±50.55*	4.5±1.6	5.25±1.79	18.2±6.7*
15	<i>m</i> -CPP + Diazepam (16)	51.0±8.02	4.5±0.64	7.25±1.03	7.25±1.25
	F (14, 60)	4.39	1.34	2.00	3.11

n = 5, Values are mean ± SEM. *P< 0.05, as compared to vehicle (ANOVA followed by Dunnett's test). O.A= Open arm, C.A= Closed arm

EAF- Ethyl acetate fraction of methanolic extract *Trigonella foenum graecum* seeds

Observation: An inverse "U" dose response [∩] curve was obtained in time spent in open arm parameter with increasing dose of EAF.

Table 28

Effect of ME, EAF, MF, PPE and KGE on Lithium sulphate (200 mg/kg, i.p) induced head twitches in rats

S.No	Treatment (mg/kg)	Number of head twitches
1	Vehicle	17.4 ± 1.20
2	ME (100)	11.5 ± 2.56*
3	EAF (30)	1 ± 0.31*
4	MF (30)	6 ± 0.70*
5	PPE (30)	11 ± 0.50*
6	KGE (30)	7 ± 0.21*

n = 5, Values are mean ± SEM. *P < 0.05, as compared to vehicle (ANOVA followed by Dunnett's test).

ME - Methanolic extract of fenugreek seeds

EAF- Ethyl acetate fraction of methanolic extract of *Trigonella foenum graecum* seeds

MF – Methanol fraction of methanolic extract of *Trigonella foenum graecum* seeds

PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes

KGE - Ethanolic extract of *Korean ginseng* roots

Table 29

Effect of PPE and KGE on Pentobarbitone (40 mg/kg, i.p) induced sleep time in mice

S.No	Treatment (mg/kg)	Sleep time (min)
1	Vehicle	123 ± 8.20
2	PPE (30)	256 ± 24.62 *
3	KGE (30)	276 ± 21.20 *

n = 5, Values are mean ± SEM. *P< 0.05, as compared to vehicle (ANOVA followed by Dunnett's test).

PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes

KGE - Ethanolic extract of *Korean ginseng* roots

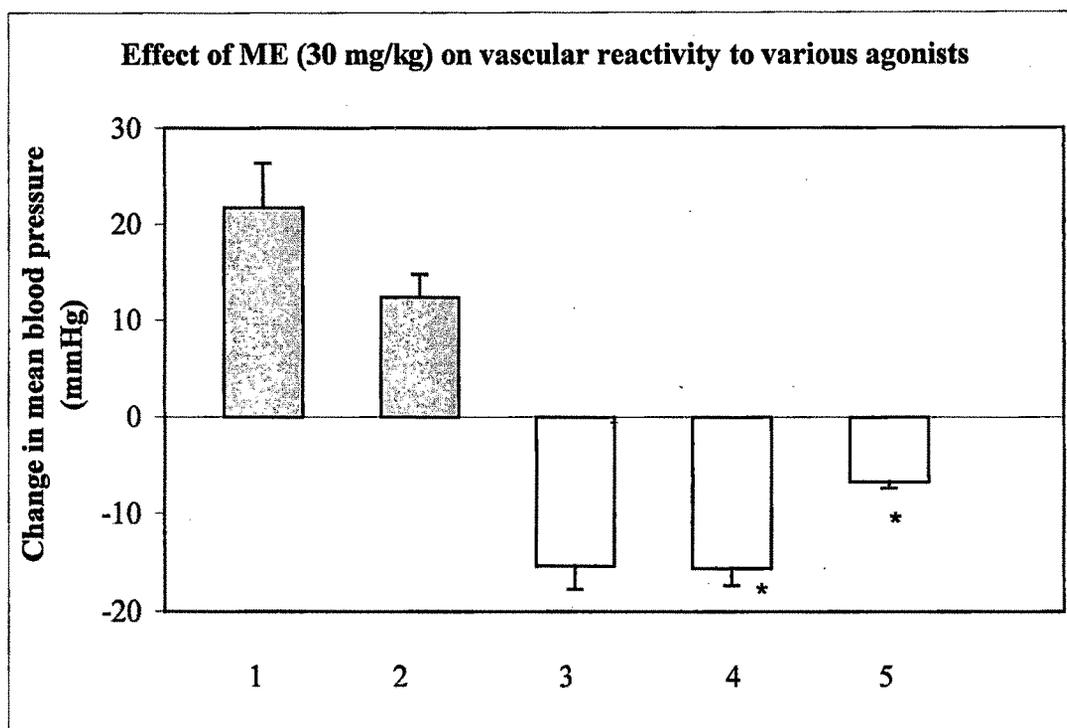
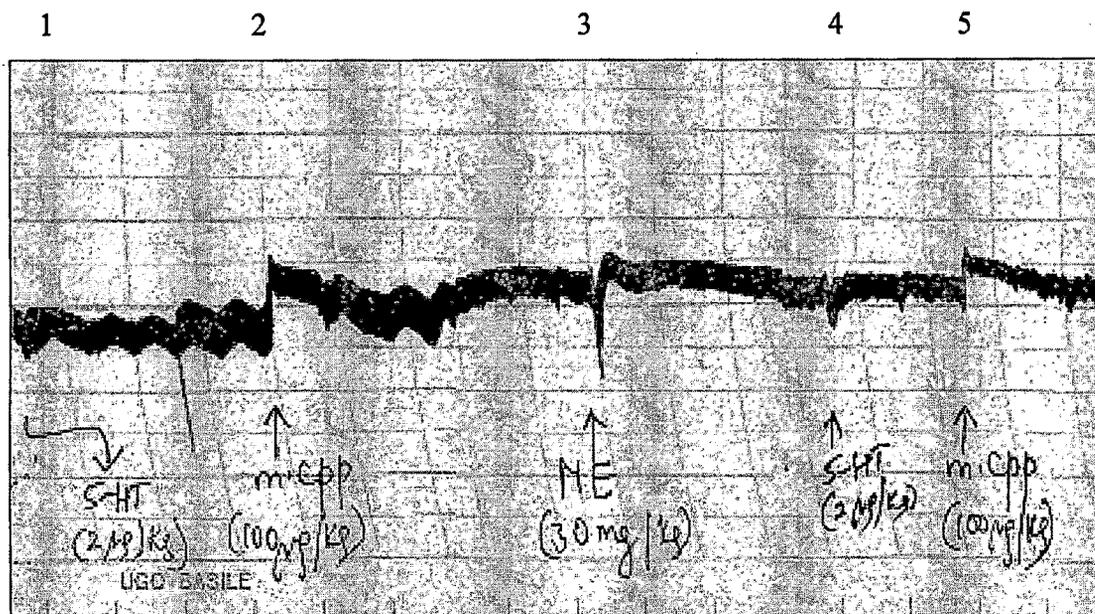


Figure 11a: Effect of ME (30 mg/kg) on vascular reactivity to various agonists in acute studies. Mean change in blood pressure (mmHg) before (1,2) and after (4,5) i.v administration of (3)- ME (30 mg/kg). (1,4)- *m*-CPP (100 µg/kg, i.v); (2,5)- 5-HT (2 µg/kg, i.v). *P<0.05 when compared to the similar previous groups. All values are expressed as mean ± SEM. Vertical lines represent SEM, n=5.

- = Rise in blood pressure
- = Fall in blood pressure

ME- Methanolic extract of *Trigonella foenum graecum* seeds



Tracing 11b: Tracing of arterial blood pressure of anaesthetized rat (urethane 120 mg/100 gm) using UGO Basile–Two Channel blood pressure recorder before (1,2) and after (4,5) i.v administration of (3)- ME (30 mg/kg). (1,4)- 5-HT (2 µg/kg, i.v); (2,5)- *m*-CPP (100 µg/kg, i.v).

Observation: A reduction in blood pressure response was noted in (4)- 5-HT (2 µg/kg, i.v) and (5)- *m*-CPP (100 µg/kg, i.v) after (3)- ME (30 mg/kg, i.v) administration.

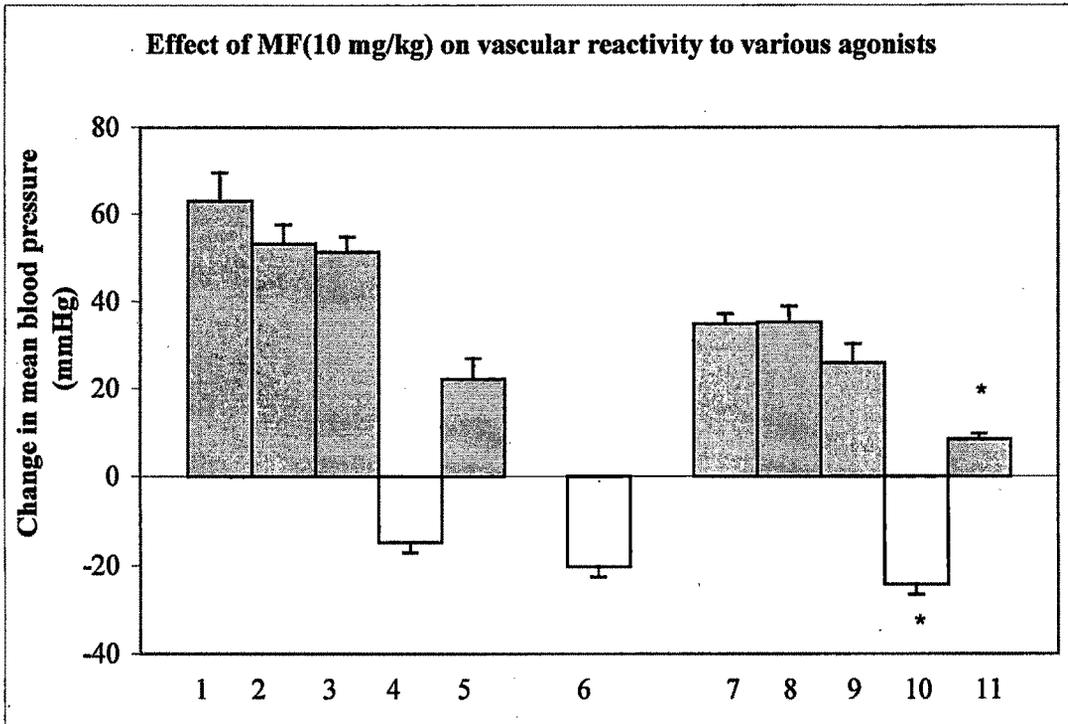
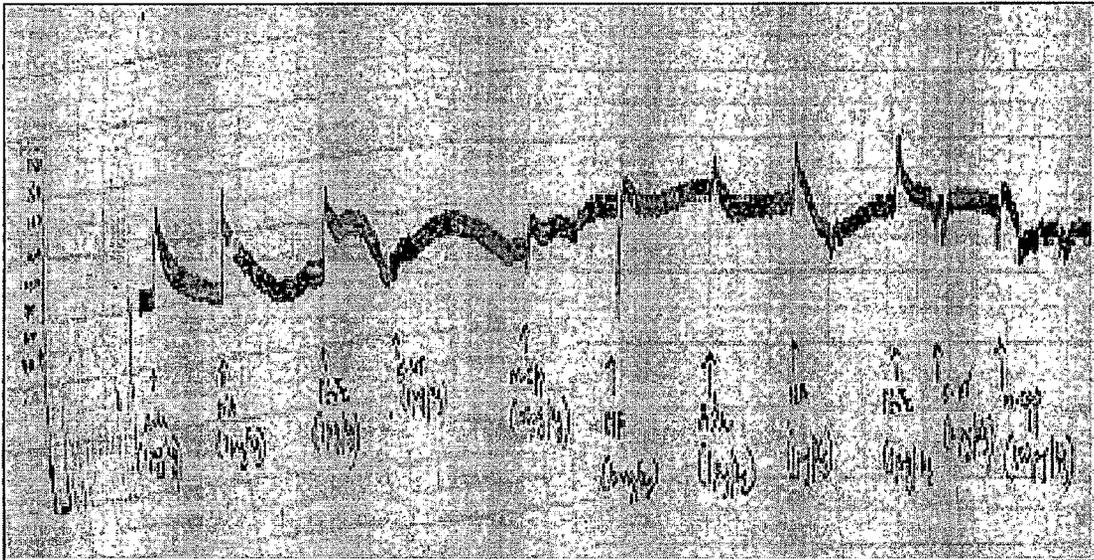


Figure 12a: Effect of MF (10 mg/kg) on vascular reactivity to various agonists in acute studies. Change in mean blood pressure (mmHg) before (1-5) and after (7-11) i.v administration of (6)- MF (10 mg/kg). (1,7)- Adr (1 μ g/kg, i.v); (2,8)- NA (1 μ g/kg, i.v); (3,9)- PhE (1 μ g/kg, i.v); (4,10)- 5-HT (1 μ g/kg, i.v); (5, 11)- *m*-CPP (100 μ g/kg, i.v). * $P < 0.05$ when compared to the similar previous groups. All values are expressed as mean \pm SEM. Vertical lines represent SEM, $n=5$.

- = Rise in blood pressure
- = Fall in blood pressure

MF- Methanolic fraction of methanolic extract of *Trigonella foenum graecum*

1 2 3 4 5 6 7 8 9 10 11



Tracing 12b: Tracing of arterial blood pressure of anaesthetized rat (urethane 120 mg/100 gm) using UGO Basile–Two Channel blood pressure recorder before (1-5) and after (7-11) i.v administration of (6)- MF (10 mg/kg). (1,7)- Adr (1 μ g/kg, i.v); (2,8)- NA (1 μ g/kg, i.v); (3,9)- PhE (1 μ g/kg, i.v); (4,10)- 5-HT (1 μ g/kg, i.v); (5,11)- *m*-CPP (100 μ g/kg, i.v).

Observation: A reduction in blood pressure response was noted in (10)- 5-HT (1 μ g/kg, i.v) and (11)- *m*-CPP (100 μ g/kg, i.v) after (6)- MF (10 mg/kg, i.v) administration.

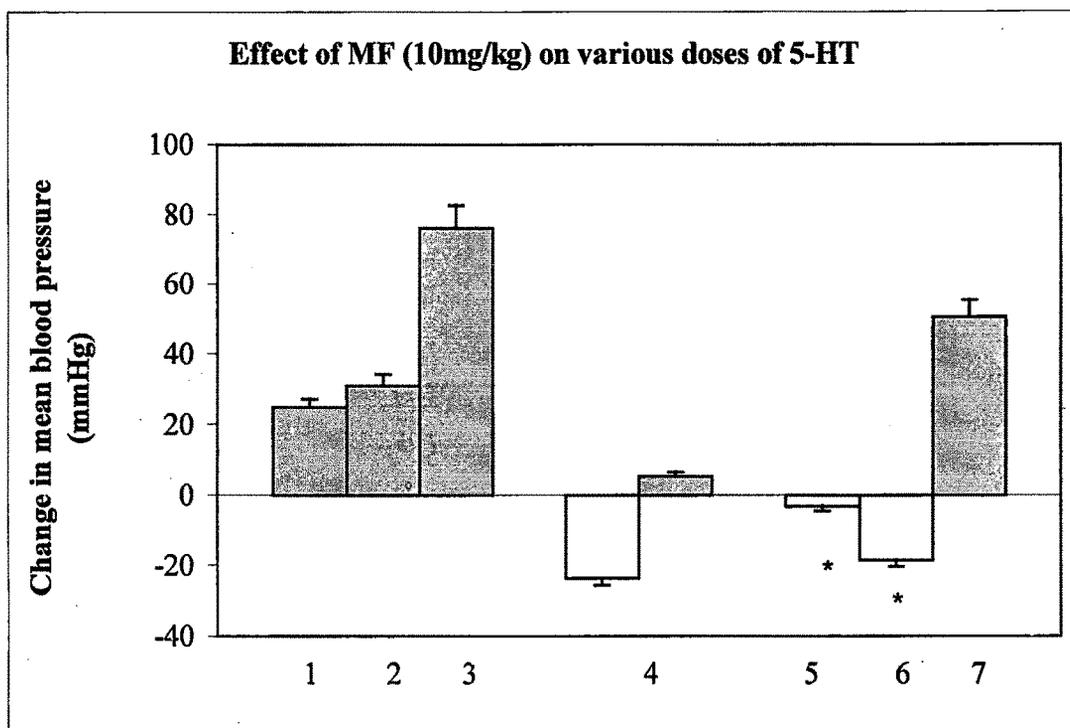
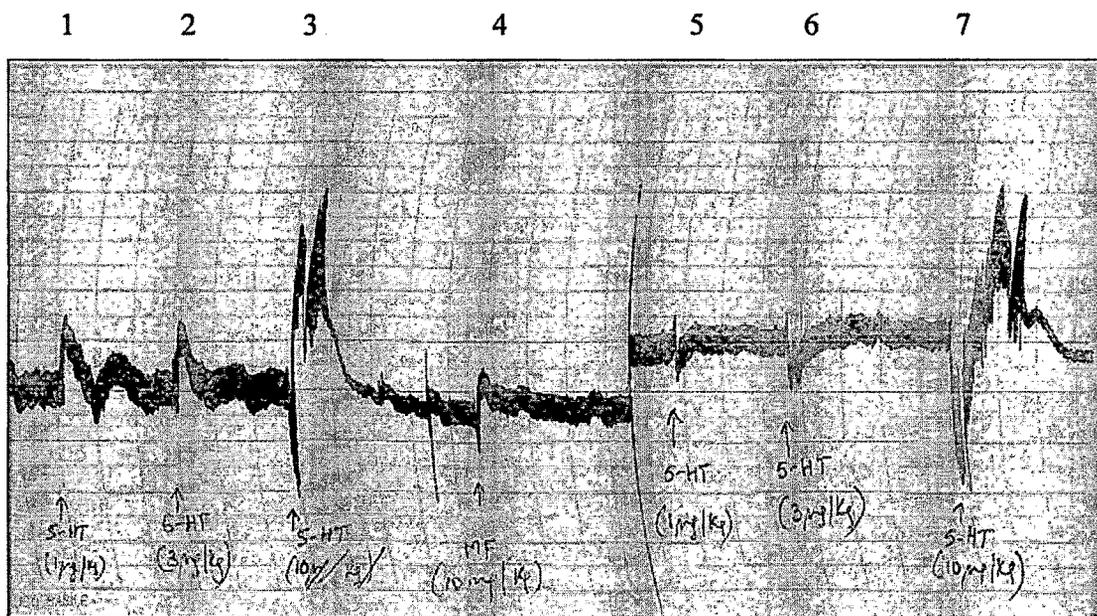


Figure 13a: Effect of MF (10 mg/kg) on vascular reactivity to various doses of 5-HT in acute studies. Change in mean blood pressure (mmHg) before (1-3) and after (5-7) i.v administration of (4)- MF (10 mg/kg). (1,5)- 5-HT (1 μ g/kg, i.v); (2,6)- 5-HT (3 μ g/kg, i.v; (3,7)- 5-HT (10 μ g/kg, i.v). *P<0.05 when compared to the similar previous groups. All values are expressed as mean \pm SEM. Vertical lines represent SEM, n=5.

- = Rise in blood pressure
- = Fall in blood pressure

MF- Methanolic fraction of methanolic extract of *Trigonella foenum graecum*



Tracing 13b: Tracing of arterial blood pressure of anaesthetized rat (urethane 120 mg/100 gm) using UGO Basile–Two Channel blood pressure recorder before (1-3) and after (5-7) i.v administration of (4)- MF (10 mg/kg). (1,5)- 5-HT (1 μg/kg, i.v); (2,6)- 5-HT (3 μg/kg, i.v); (3,7)- 5-HT (10 μg/kg, i.v).

Observation: A reversal in blood pressure response was noted in (5)- 5-HT (1 μg/kg, i.v) and (6)- 5-HT (3 μg/kg, i.v) after (3)- MF (10 mg/kg, i.v) administration.

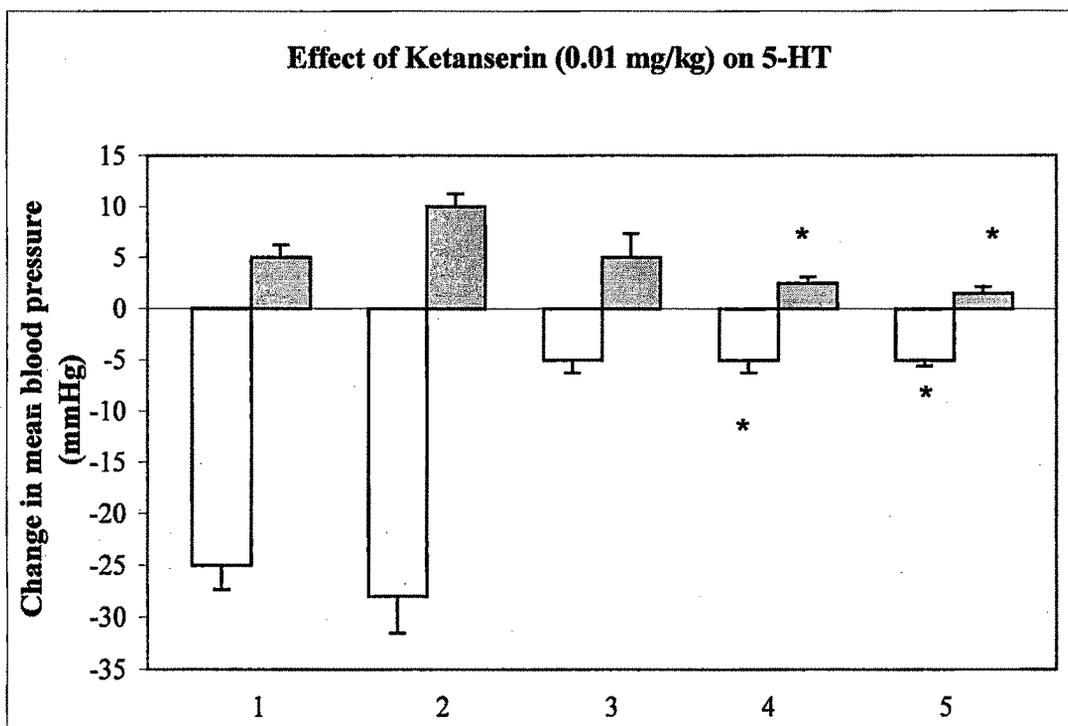
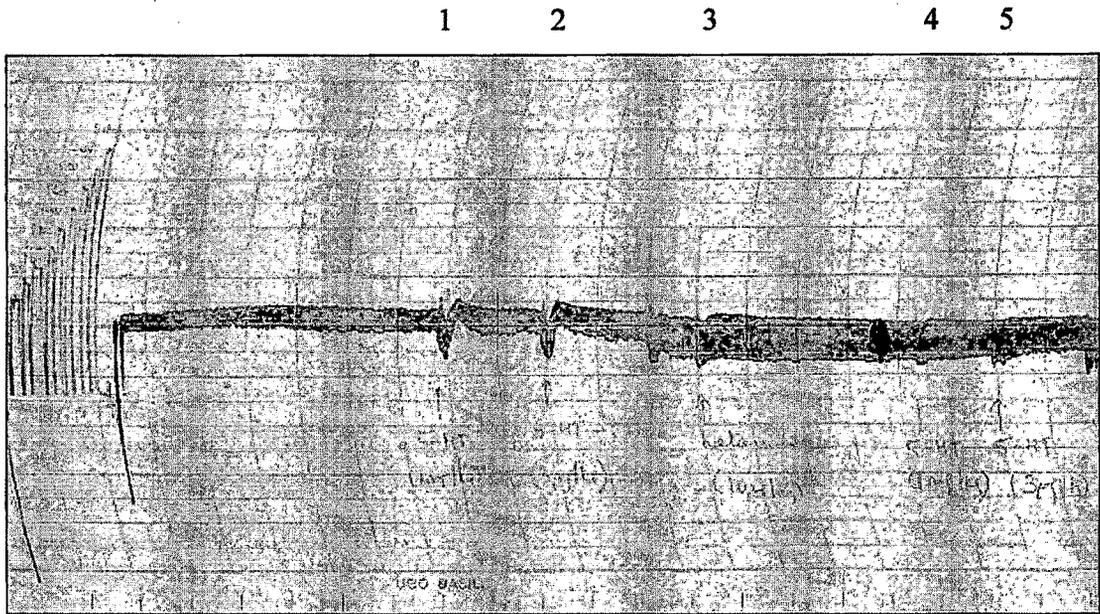


Figure 14a: Effect of Ketanserin (10 μ g/kg, i.v.) on vascular reactivity to various doses of 5-HT. Mean change in blood pressure (mmHg) before (1,2) and after (4,5) i.v administration of (3)- Ketanserin (10 μ g/kg). (1,4)- 5-HT (1 μ g/kg, i.v); (2,5)- 5-HT (3 μ g/kg, i.v). * $P < 0.05$ when compared to the similar previous groups. All values are expressed as mean \pm SEM. Vertical lines represent SEM, n=5.

- = Rise in blood pressure
- = Fall in blood pressure



Tracing 14b: Tracing of arterial blood pressure of anaesthetized rat (urethane 120 mg/100 gm) using UGO Basile–Two Channel blood pressure recorder before (1,2) and after (4,5) i.v administration of (3)- Ketanserin (10 $\mu\text{g}/\text{kg}$). (1,4)- 5-HT (1 $\mu\text{g}/\text{kg}$, i.v); (2,5)- 5-HT (3 $\mu\text{g}/\text{kg}$, i.v).

Observation: A blockade in blood pressure response was noted in (4)- 5-HT (1 $\mu\text{g}/\text{kg}$, i.v) and (5)- 5-HT (3 $\mu\text{g}/\text{kg}$, i.v) after (3)- Ketanserin (10 $\mu\text{g}/\text{kg}$, i.v) administration.

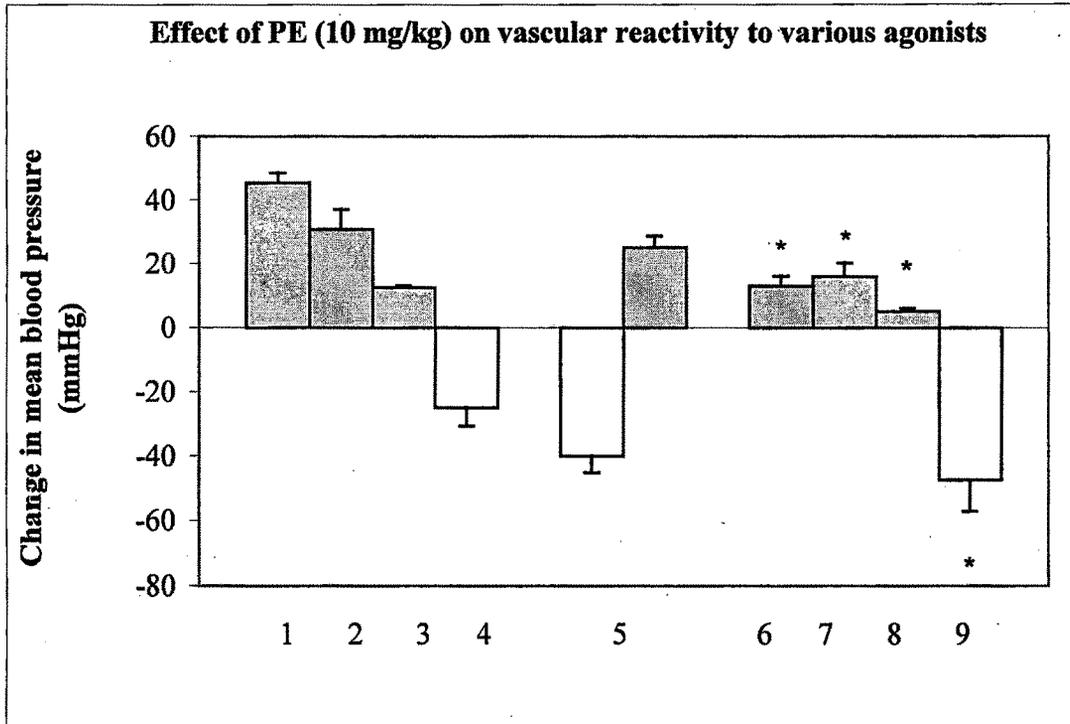
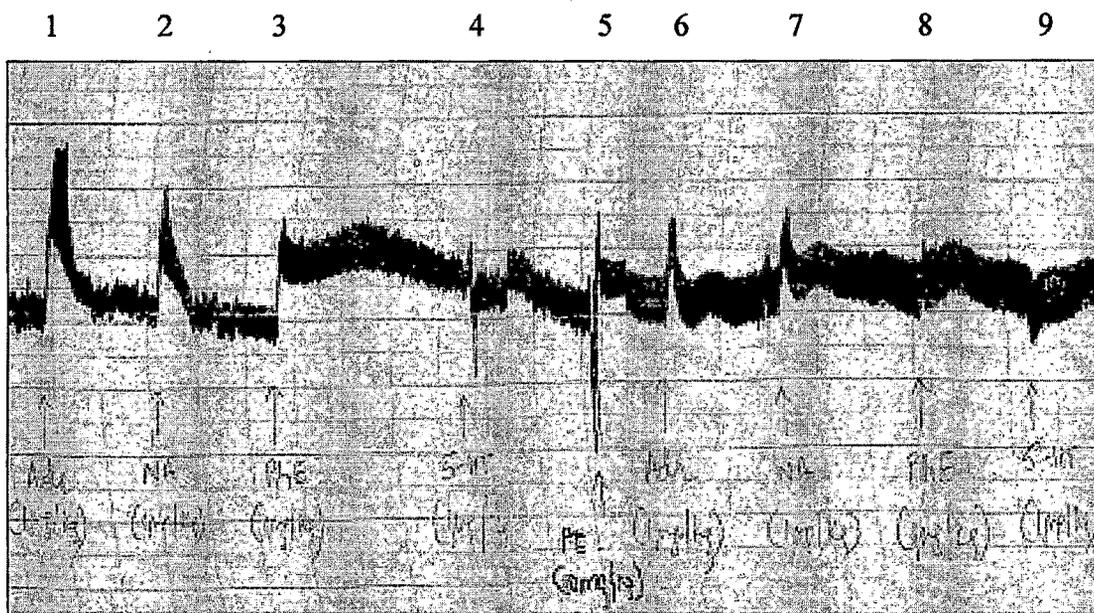


Figure 15a: Effect of PE (10 mg/kg) on vascular reactivity to various agonists in acute studies. Change in mean blood pressure (mmHg) before (1-4) and after (6-9) i.v administration of (5)- PE (10 mg/kg). (1,6)- Adr (1 μ g/kg, i.v); (2,7)- NA (1 μ g/kg, i.v); (3,8)- PhE (1 μ g/kg, i.v); (4,9)- 5-HT (1 μ g/kg, i.v). *P<0.05 when compared to the similar previous groups. All values are expressed as mean \pm SEM. Vertical lines represent SEM, n=5.

- = Rise in blood pressure
- = Fall in blood pressure

PE- Pet ether extract of *Zingiber officinale*



Tracing 15b: Tracing of arterial blood pressure of anaesthetized rat (urethane 120 mg/100 gm) using UGO Basile–Two Channel blood pressure recorder before (1-4) and after (6-9) i.v administration of (5)- PE (10 mg/kg). (1,6)- Adr (1µg/kg, i.v); (2,7)- NA (1µg/kg, i.v); (3,8)- PhE (1µg/kg, i.v); (4,9)- 5-HT (1µg/kg, i.v).

Observation: A reduction in blood pressure response was noted in (6)- Adr (1µg/kg, i.v); (7)- NA (1µg/kg, i.v); (8)- PhE (1µg/kg, i.v); (9)- 5-HT (1µg/kg, i.v) after (5)- PE (10 mg/kg, i.v) administration.

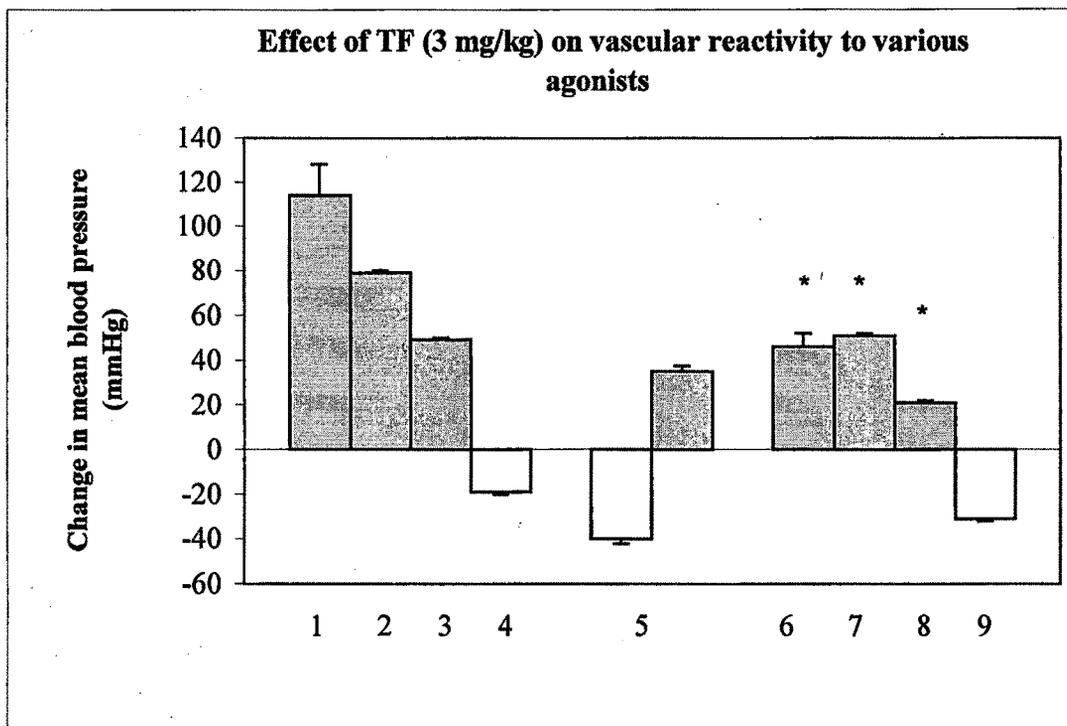
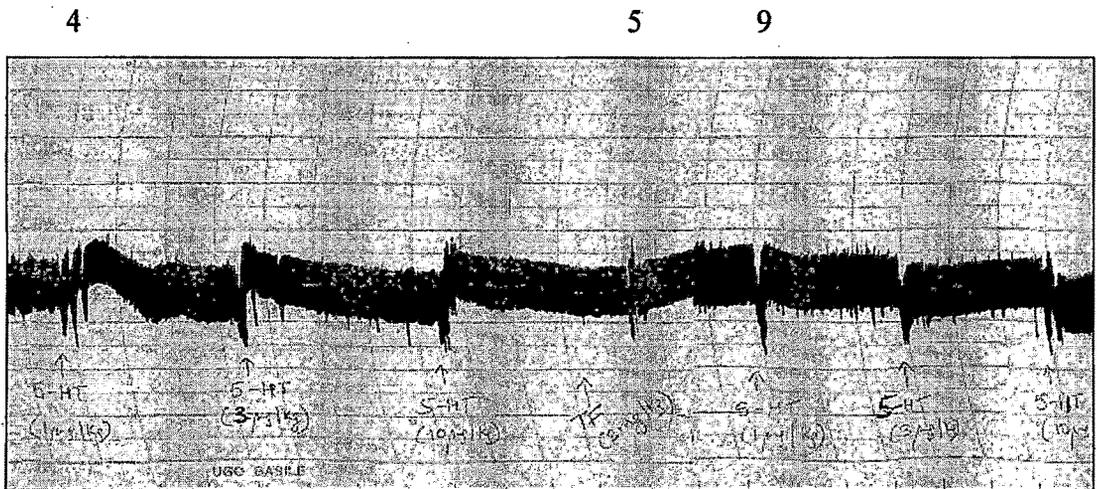
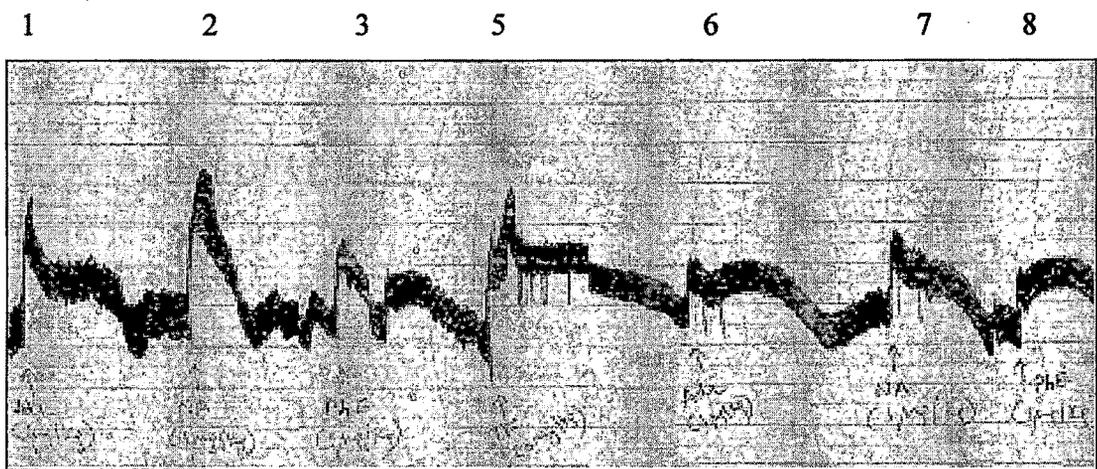


Figure 16a: Effect of TF (3mg/kg) on vascular reactivity to various agonists in acute studies. Change in mean blood pressure (mmHg) before (1-4) and after (6-9) i.v administration of (5)- TF (3 mg/kg). (1,6)- Adr (1 μ g/kg, i.v); (2,7)- NA (1 μ g/kg, i.v); (3,8)- PhE (1 μ g/kg, i.v); (4,9)- 5-HT (1 μ g/kg, i.v). *P<0.05 when compared to the similar previous groups. All values are expressed as mean \pm SEM. Vertical lines represent SEM, n=5.

- = Rise in blood pressure
- = Fall in blood pressure

TF- Toluene fraction of Petroleum ether extract of *Zingiber officinale*



Tracing 16b: Tracing of arterial blood pressure of anaesthetized rat (urethane 120 mg/100 gm) using UGO Basile–Two Channel blood pressure recorder before (1-4) and after (6-9) i.v administration of (5)- TF (3 mg/kg). (1,6)- Adr (1 μ g/kg, i.v); (2,7)- NA (1 μ g/kg, i.v); (3,8)- PhE (1 μ g/kg, i.v); (4,9)- 5-HT (1 μ g/kg, i.v).

Observation: A reduction in blood pressure response was noted in (6)- Adr (1 μ g/kg, i.v); (7)- NA (1 μ g/kg, i.v); (8)- PhE (1 μ g/kg, i.v) after (5)- TF (3 mg/kg, i.v) administration.

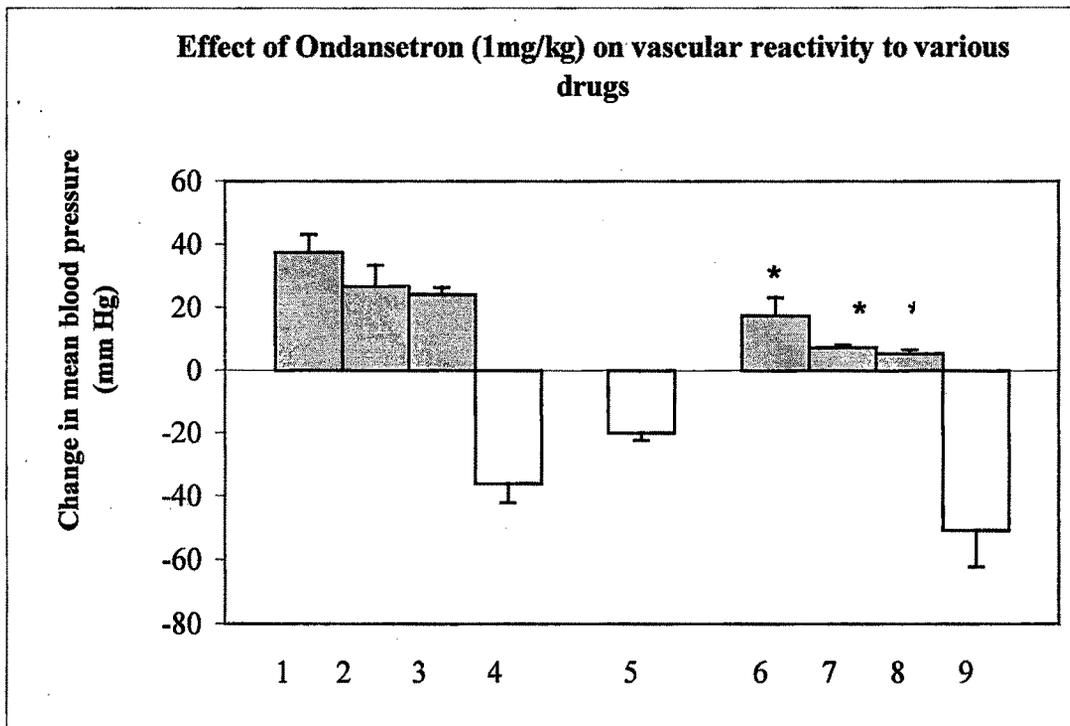
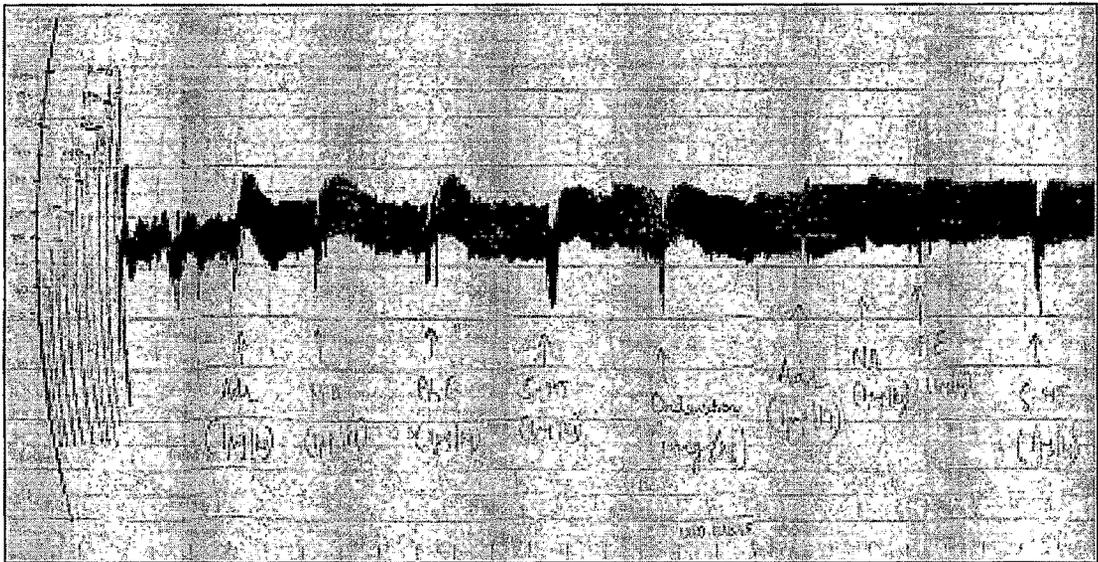


Figure 17a: Effect of Ondansetron (1mg/kg) on vascular reactivity to various agonists. Change in mean blood pressure (mmHg) before (1-4) and after (6-9) i.v administration of (5)- Ondansetron (1mg/kg). (1,6)- Adr (1 μ g/kg, i.v); (2,7)- NA (1 μ g/kg, i.v); (3,8)- PhE (1 μ g/kg, i.v); (4,9)- 5-HT (1 μ g/kg, i.v). *P<0.05 when compared to the similar previous groups. All values are expressed as mean \pm SEM. Vertical lines represent SEM, n=5.

- = Rise in blood pressure
- = Fall in blood pressure

1 2 3 4 5 6 7 8 9



Tracing 17b: Tracing of arterial blood pressure of anaesthetized rat (urethane 120 mg/100 gm) using UGO Basile–Two Channel blood pressure recorder before (1-4) and after (6-9) i.v administration of (5)- Ondansetron (1mg/kg). (1,6)- Adr (1 μ g/kg, i.v); (2,7)- NA (1 μ g/kg, i.v); (3,8)- PhE (1 μ g/kg, i.v); (4,9)- 5-HT (1 μ g/kg, i.v).

Observation: A reduction in blood pressure response was noted in (6)- Adr (1 μ g/kg, i.v); (7)- NA (1 μ g/kg, i.v); (8)- PhE (1 μ g/kg, i.v) after (5)- Ondansetron (1 mg/kg, i.v) administration.

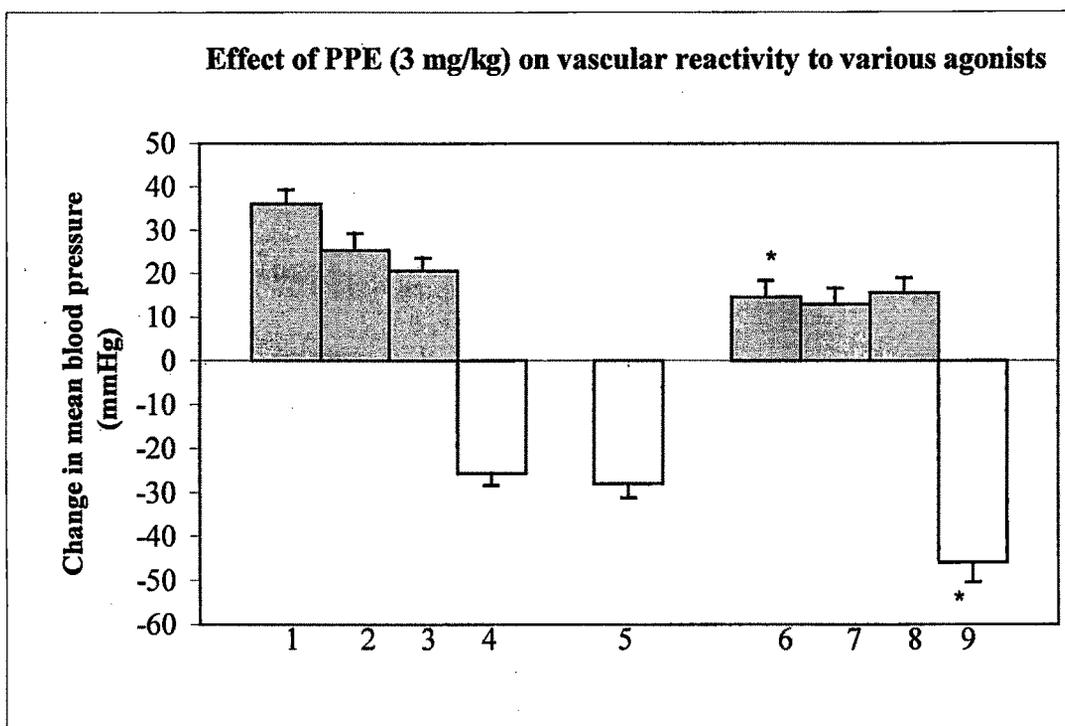
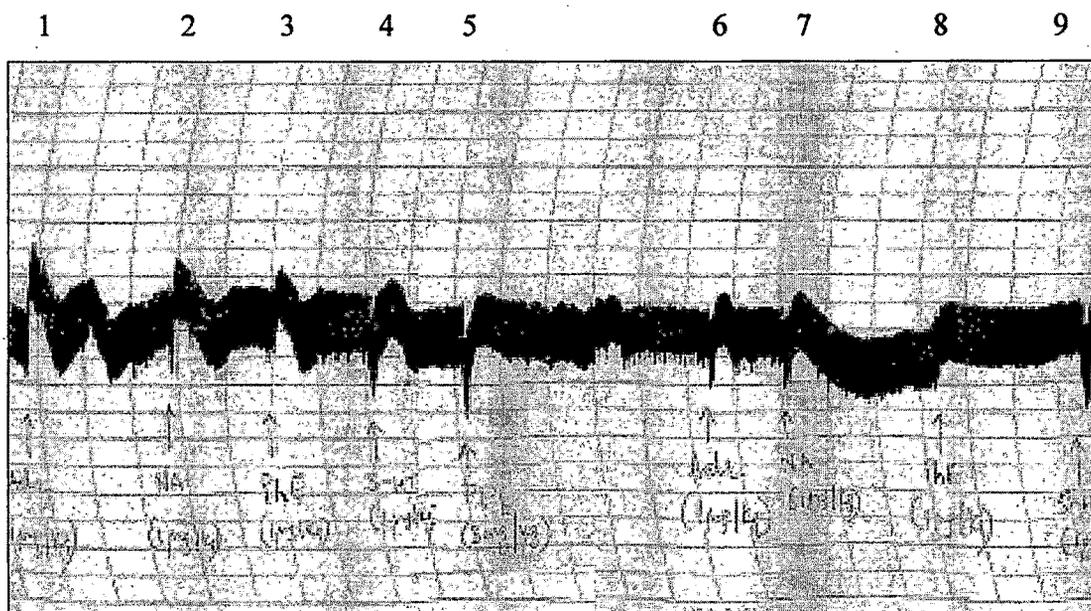


Figure 18a: Effect of PPE (3mg/kg) on vascular reactivity to various agonists. Change in mean blood pressure (mmHg) before (1-4) and after (6-9) i.v administration of (5)- PPE (3 mg/kg). (1,6)- Adr (1 μ g/kg, i.v); (2,7)- NA (1 μ g/kg, i.v); (3,8)- PhE (1 μ g/kg, i.v); (4,9)- 5-HT (1 μ g/kg, i.v). *P<0.05 when compared to the similar previous groups. All values are expressed as mean \pm SEM. Vertical lines represent SEM, n=5.

- = Rise in blood pressure
- = Fall in blood pressure

PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes



Tracing 18b: Tracing of arterial blood pressure of anaesthetized rat (urethane 120 mg/100 gm) using UGO Basile–Two Channel blood pressure recorder before (1-4) and after (6-9) i.v administration of (5)- PPE (3 mg/kg). (1,6)- Adr (1 μ g/kg, i.v); (2,7)- NA (1 μ g/kg, i.v); (3,8)- PhE (1 μ g/kg, i.v); (4,9)- 5-HT (1 μ g/kg, i.v).

Observation: A reduction in blood pressure response was noted in (6)- Adr (1 μ g/kg, i.v); (9)- 5-HT- (1 μ g/kg, i.v) after (5)- PPE (3 mg/kg, i.v) administration.

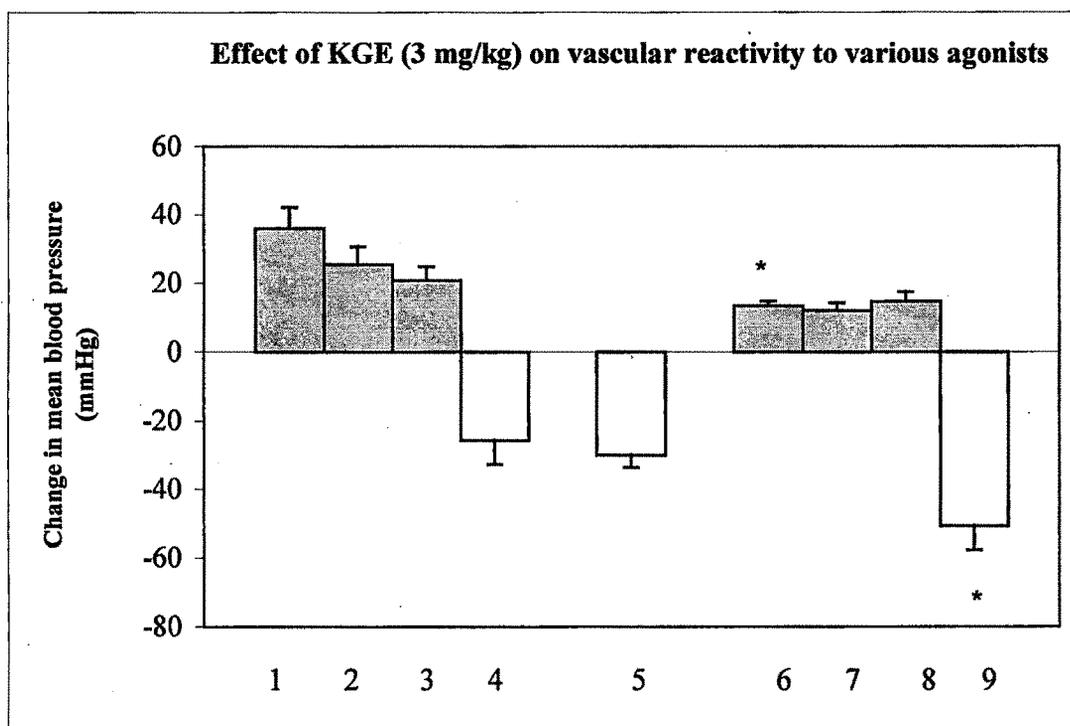
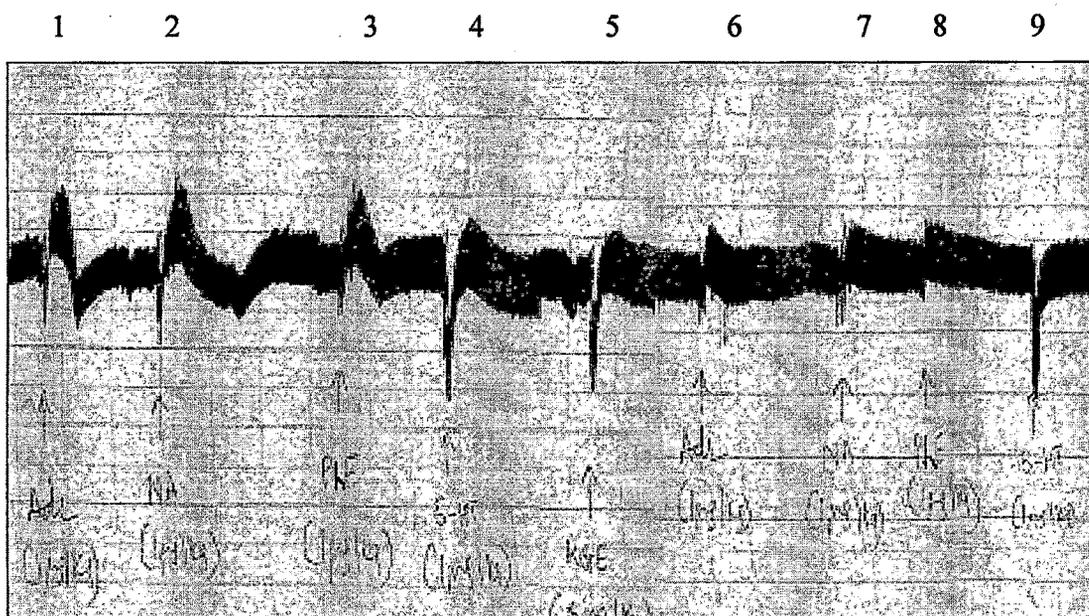


Figure 19a: Effect of KGE (3mg/kg) on vascular reactivity to various agonists. Change in mean blood pressure (mmHg) before (1-4) and after (6-9) i.v administration of (5)- KGE (3 mg/kg). (1,6)- Adr (1 μ g/kg, i.v); (2,7)- NA (1 μ g/kg, i.v); (3,8)- PhE (1 μ g/kg, i.v); (4,9)- 5-HT (1 μ g/kg, i.v). *P<0.05 when compared to the similar previous groups. All values are expressed as mean \pm SEM. Vertical lines represent SEM, n=5.

- = Rise in blood pressure
- = Fall in blood pressure

KGE - Ethanolic extract of *Korean ginseng* roots



Tracing 19b: Tracing of arterial blood pressure of anaesthetized rat (urethane 120 mg/100 gm) using UGO Basile–Two Channel blood pressure recorder before (1-4) and after (6-9) i.v administration of (5)- KGE (3 mg/kg). (1,6)- Adr (1µg/kg, i.v); (2,7)- NA (1µg/kg, i.v); (3,8)- PhE (1µg/kg, i.v); (4,9)- 5-HT (1µg/kg, i.v).

Observation: A reduction in blood pressure response was noted in (6)- Adr (1µg/kg, i.v); (9)- 5-HT- (1µg/kg, i.v) after (5)- KGE (3 mg/kg, i.v) administration.

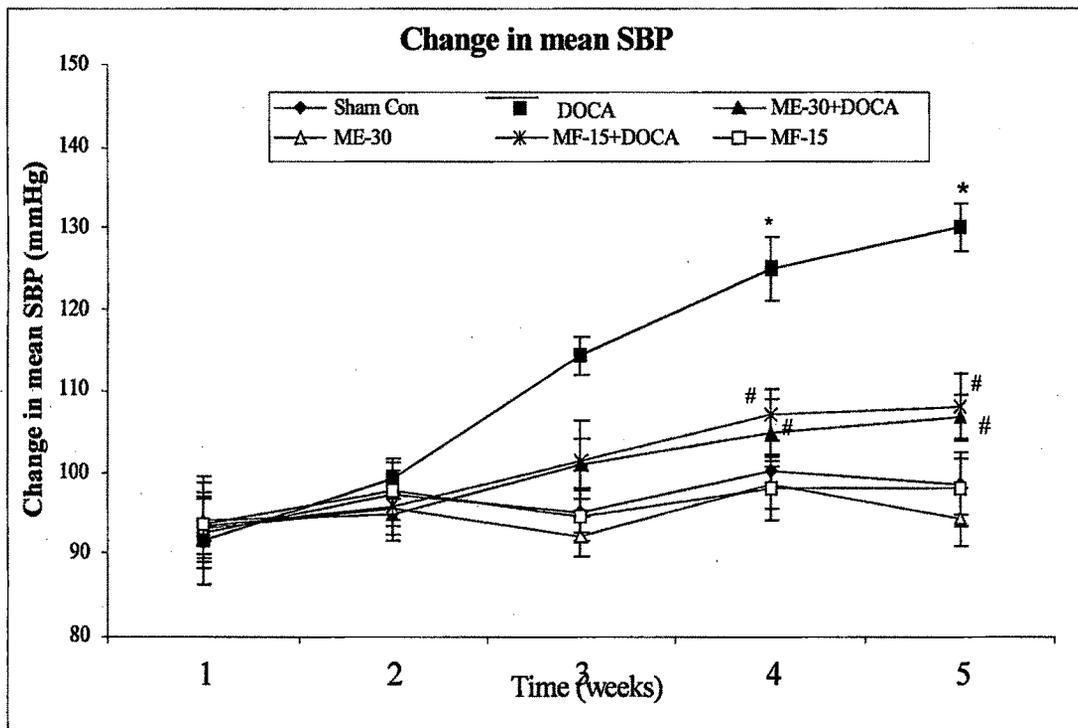


Figure 20: Time course (weekly) of changes in systolic blood pressure (mmHg) during 5 weeks treatment schedule in Sham control, DOCA, ME-30+DOCA, ME-30, MF-15 +DOCA, MF-15 treated groups. *P<0.05 when compared to sham control group.

#P<0.05 when compared to DOCA hypertensive rats. All values are expressed as mean \pm SEM. Vertical lines represent SEM, n=6.

SBP- Systolic blood pressure

ME- Methanolic extract of *Trigonella foenum graecum*

MF- Methanolic fraction of methanolic extract of *Trigonella foenum graecum*

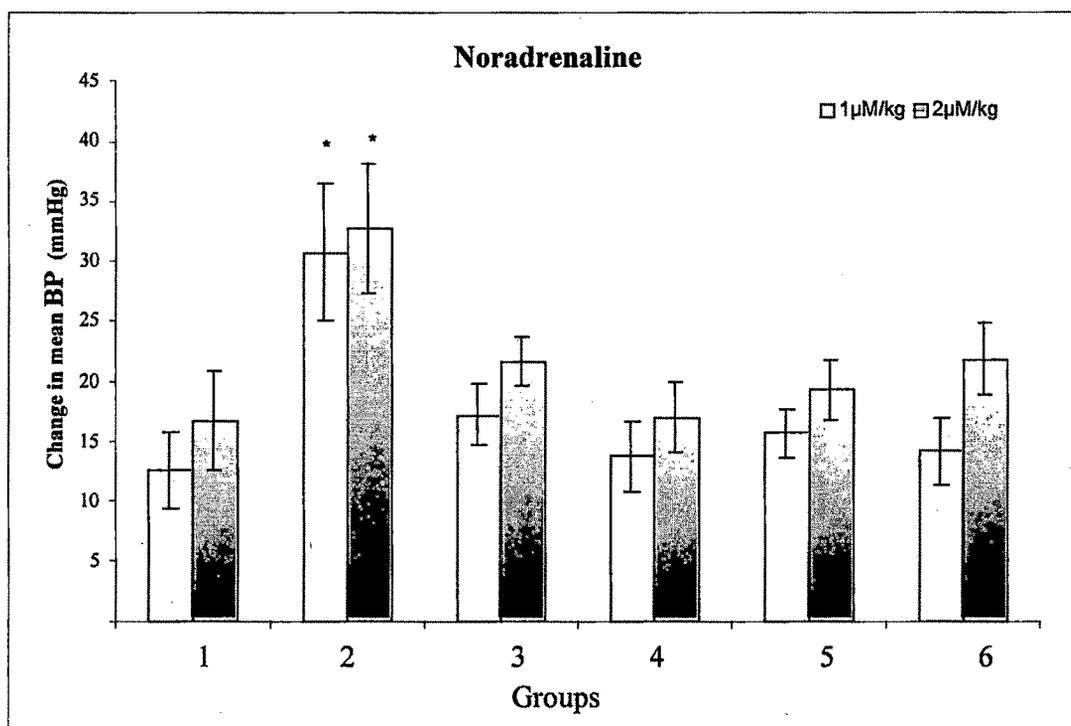


Figure 21a: Change in mean blood pressure to Noradrenaline (1 $\mu\text{M}/\text{kg}$, i.v; 2 $\mu\text{M}/\text{kg}$, i.v) in (1)- Sham control, (2)- DOCA, (3)- ME-30+DOCA, (4)- ME-30, (5)- MF-15 +DOCA, (6)- MF-15 treated groups after completion of 4-week treatment schedule. * $P < 0.05$ when compared to sham control rats. All values are expressed as mean \pm SEM. Vertical lines represent SEM, $n=6$.

BP- Blood pressure

ME- Methanolic extract of *Trigonella foenum graecum*

MF- Methanolic fraction of methanolic extract of *Trigonella foenum graecum*

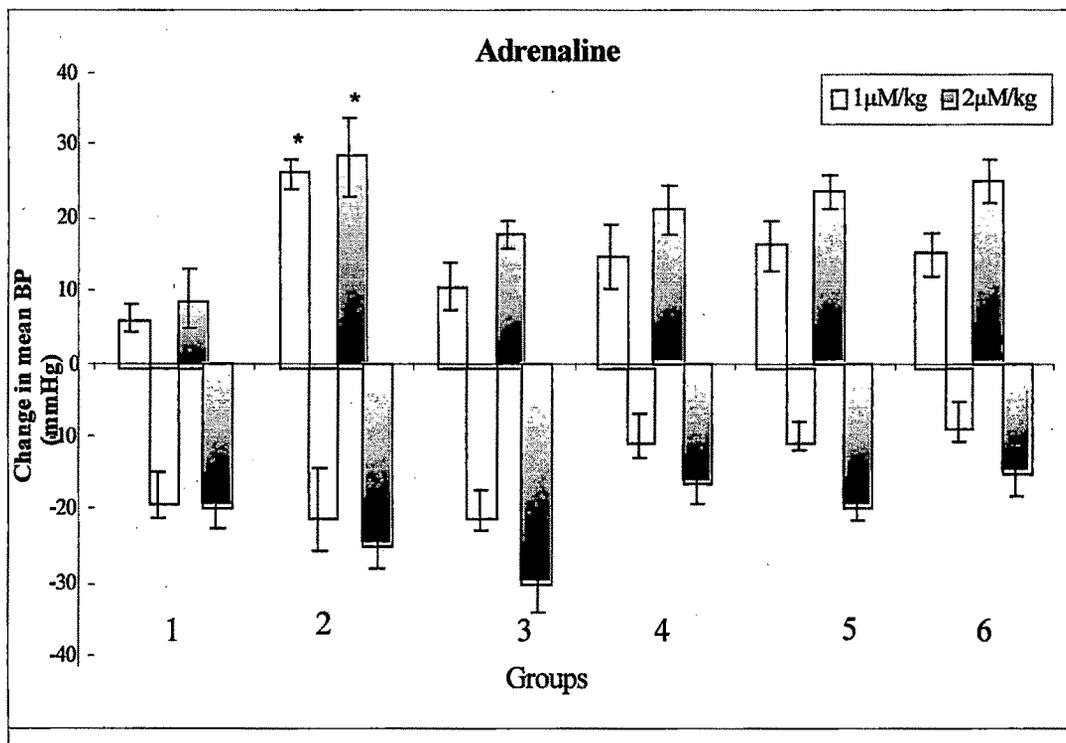


Figure 22a: Change in mean blood pressure to Adrenaline (1 $\mu\text{M}/\text{kg}$, i.v; 2 $\mu\text{M}/\text{kg}$, i.v) in (1)- Sham control, (2)- DOCA, (3)- ME-30+DOCA, (4)- ME-30, (5)- MF-15 +DOCA, (6)- MF-15 treated groups after completion of 4-week treatment schedule. * $P < 0.05$ when compared to sham control rats. All values are expressed as mean \pm SEM. Vertical lines represent SEM, $n=6$.

BP- Blood pressure

ME- Methanolic extract of *Trigonella foenum graecum*

MF- Methanolic fraction of methanolic extract of *Trigonella foenum graecum*

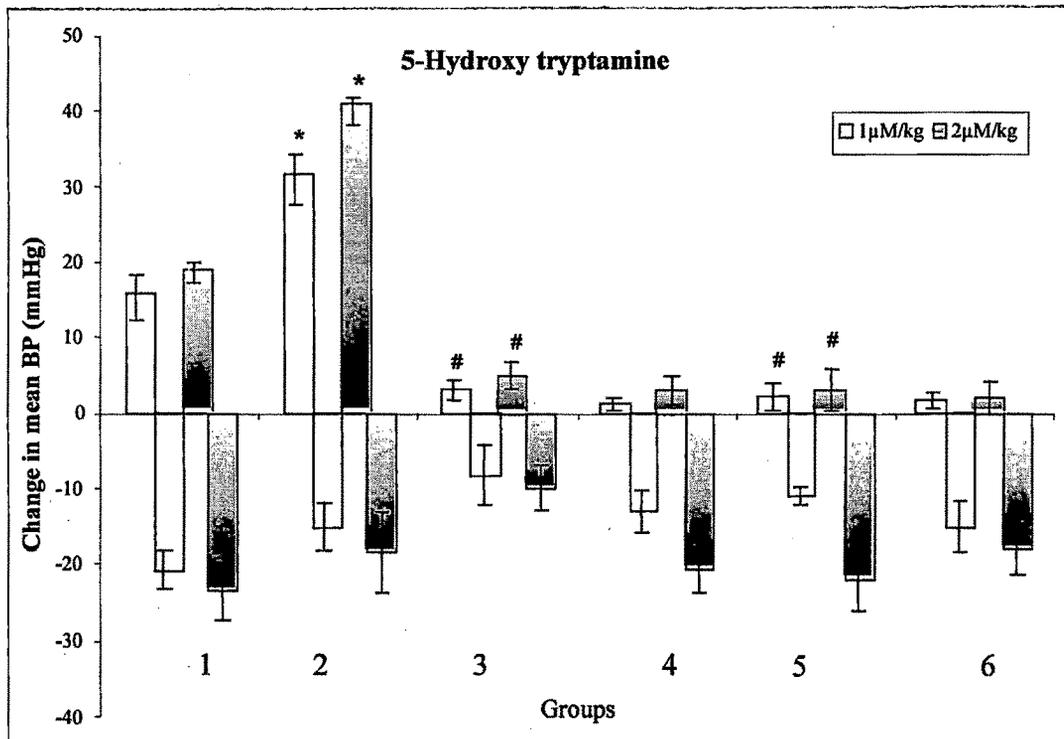


Figure 23a: Change in mean blood pressure to 5-HT (1 $\mu\text{M}/\text{kg}$, i.v; 2 $\mu\text{M}/\text{kg}$, i.v) in (1)- Sham control, (2)- DOCA, (3)- ME-30+DOCA, (4)- ME-30, (5)- MF-15 +DOCA, (6)- MF-15 treated groups after completion of 4-week treatment schedule. * $P < 0.05$ when compared to sham control and # $P < 0.05$ when compared to DOCA hypertensive rats. All values are expressed as mean \pm SEM. Vertical lines represent SEM, $n=6$.

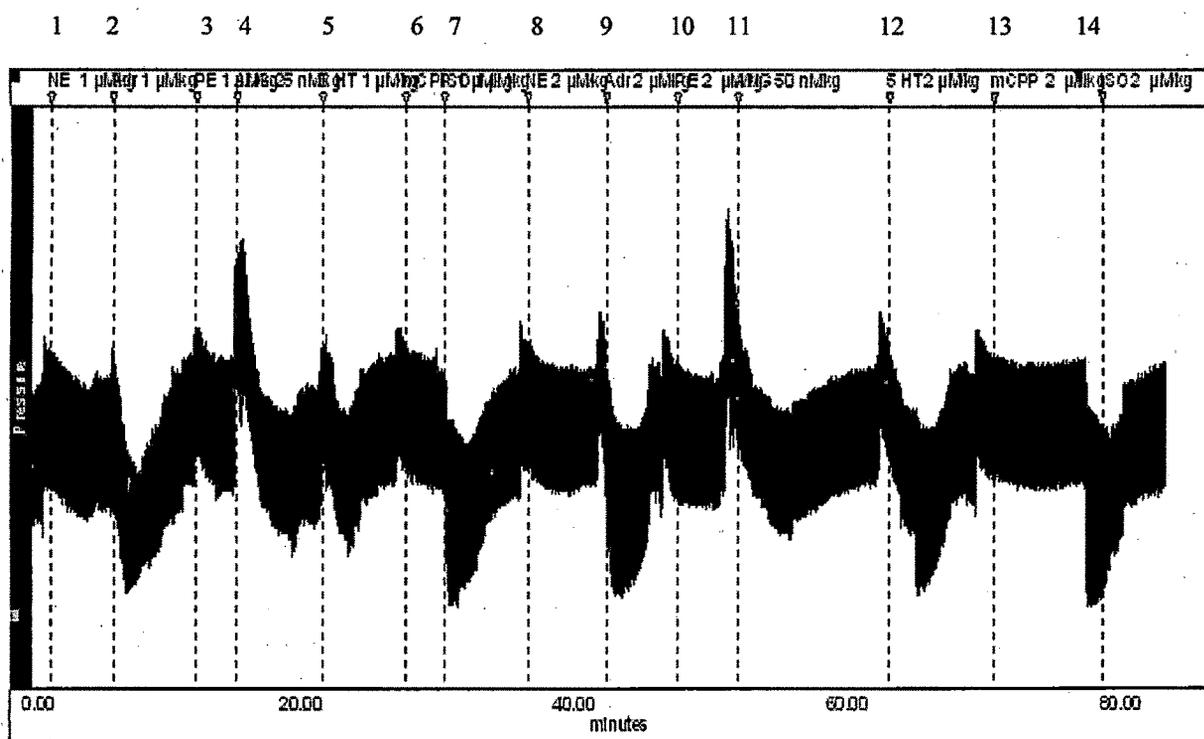
BP- Blood pressure

ME- Methanolic extract of *Trigonella foenum graecum*

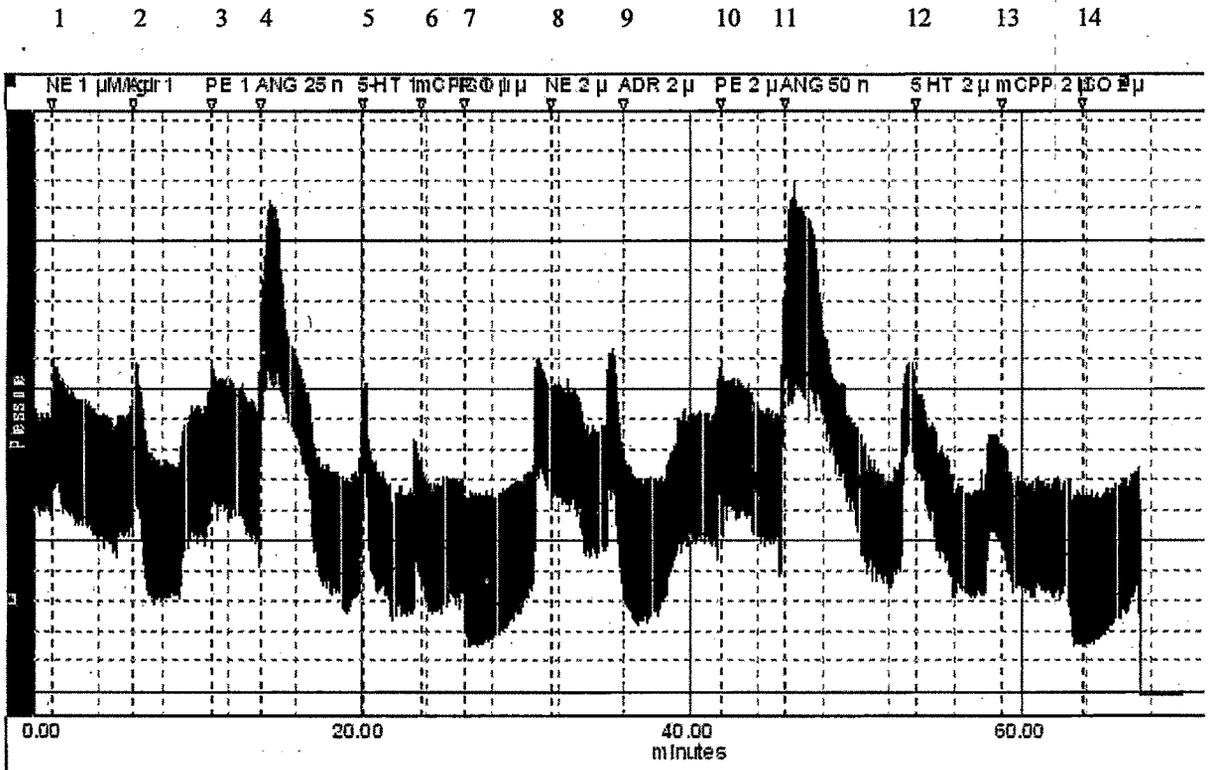
MF- Methanolic fraction of methanolic extract of *Trigonella foenum graecum*

Tracing 21b, 22b, 23b: Tracing of arterial blood pressure of anaesthetized rat (urethane 120 mg/100 gm) using BIOPAC Data Acquisition System (BIOPAC MP30 SYSTEM, USA) blood pressure recorder after intravenous administration of [1,8]-noradrenaline (1, 2 μ M/kg); [2,9]-adrenaline (1, 2 μ M/kg); [3,10]-phenylephrine (1, 2 μ M/kg); [4,11]-angiotensin-II (25, 50 nM/kg); [5,12]- 5-Hydroxy tryptamine (1, 2 μ M/kg); [6,13]- *m*-CPP (1, 2 μ M/kg); and [7,14]- isoprenaline (1, 2 μ M/kg) in (A) Sham operated control rats, (B) DOCA-salt hypertensive rats, (C) ME (30 mg/kg) treated DOCA hypertensive rats (D) ME (30 mg/kg) treated control rats (E) MF (15 mg/kg) treated DOCA hypertensive rats (F) MF (15 mg/kg) treated control rats. [1-7]= (1 μ M/kg); [8-14]= (2 μ M/kg).

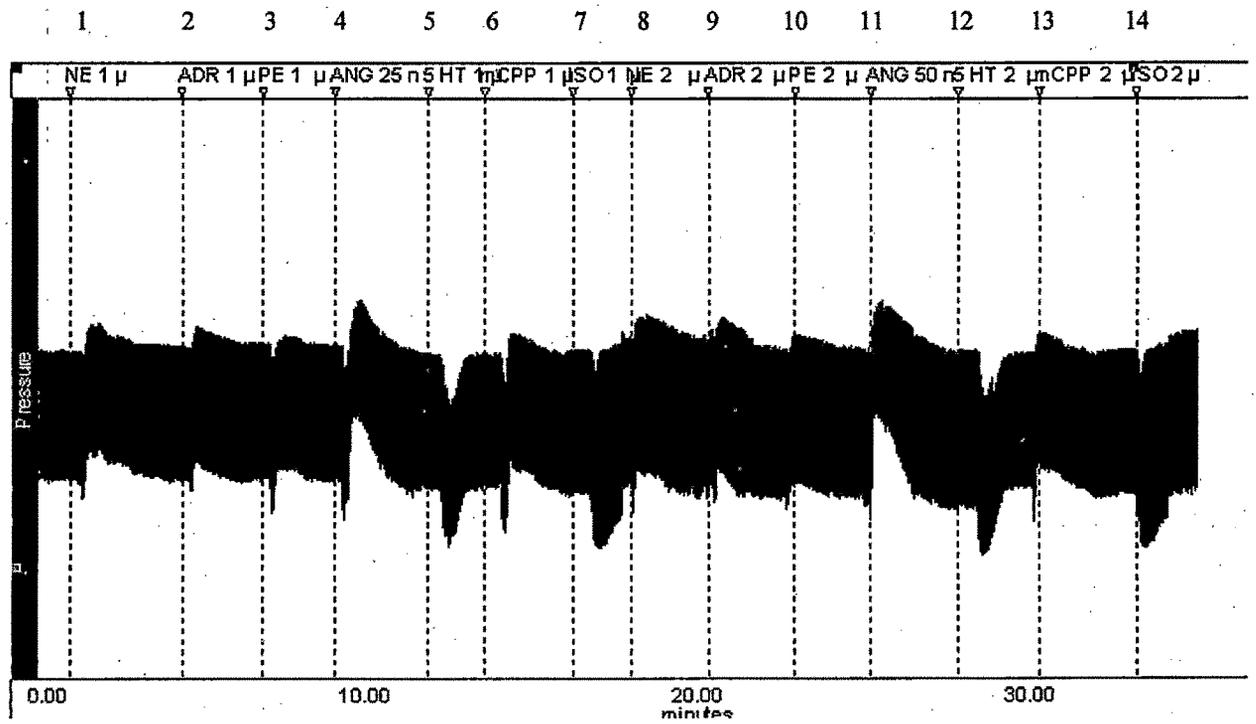
A)



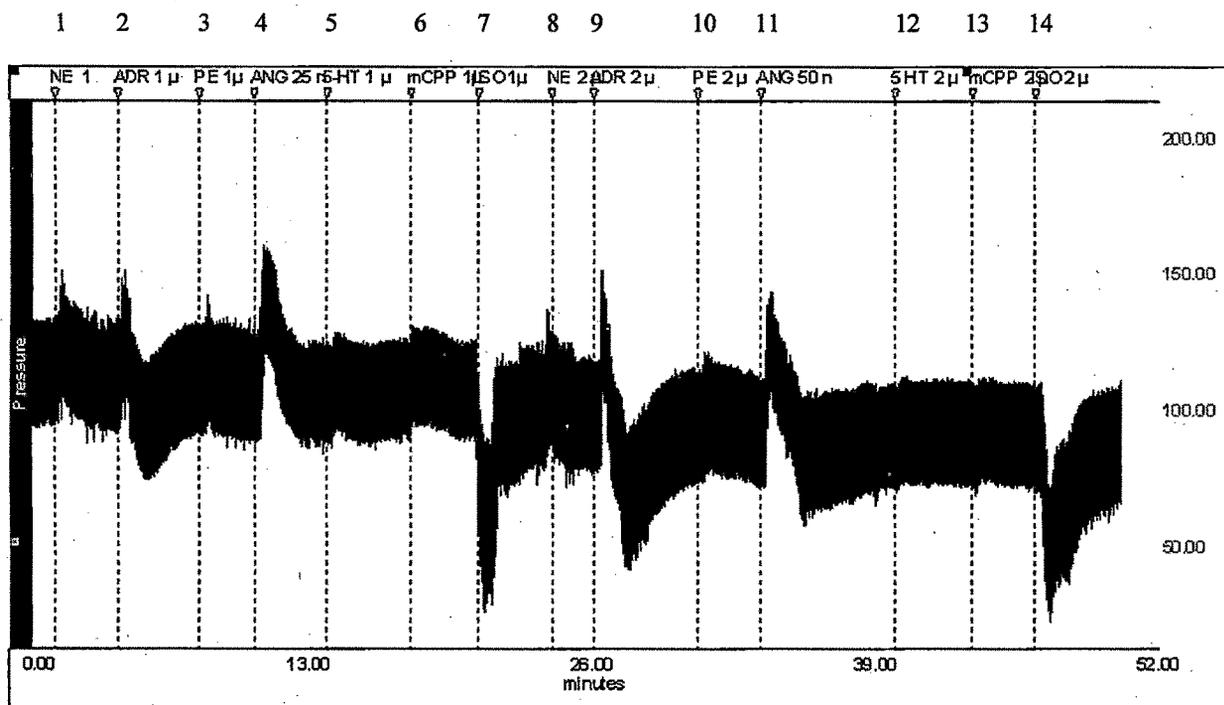
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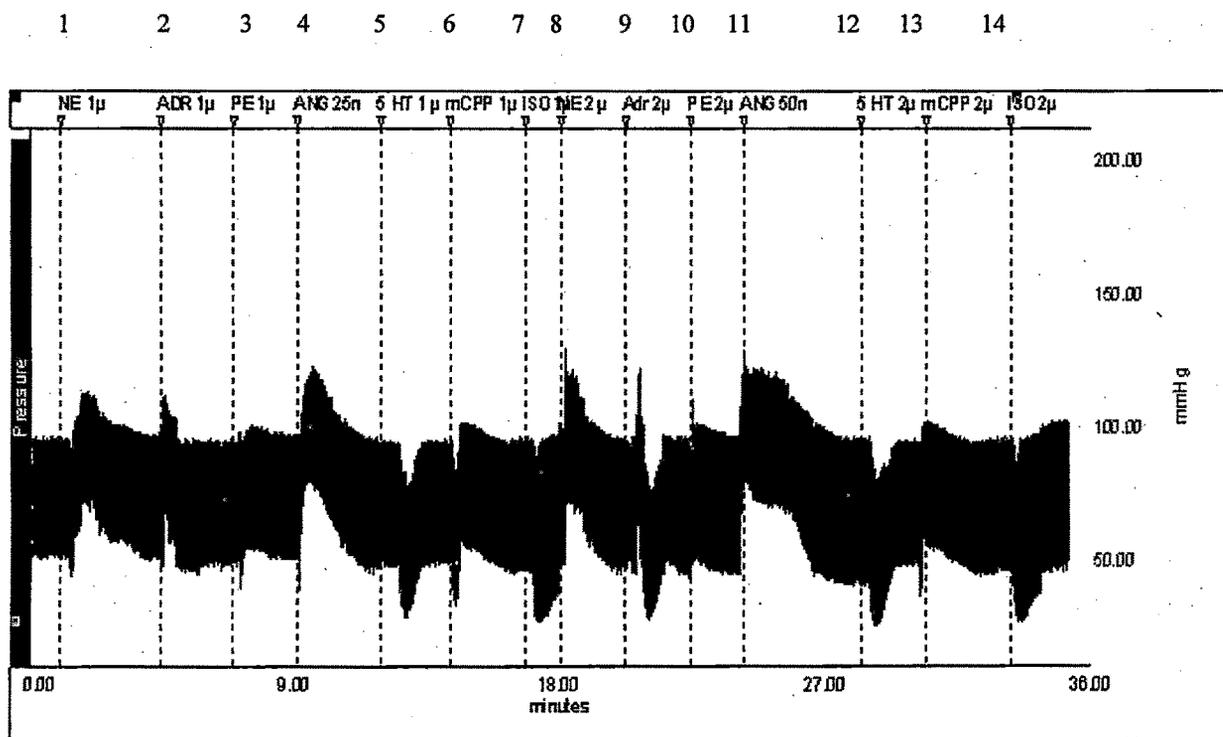
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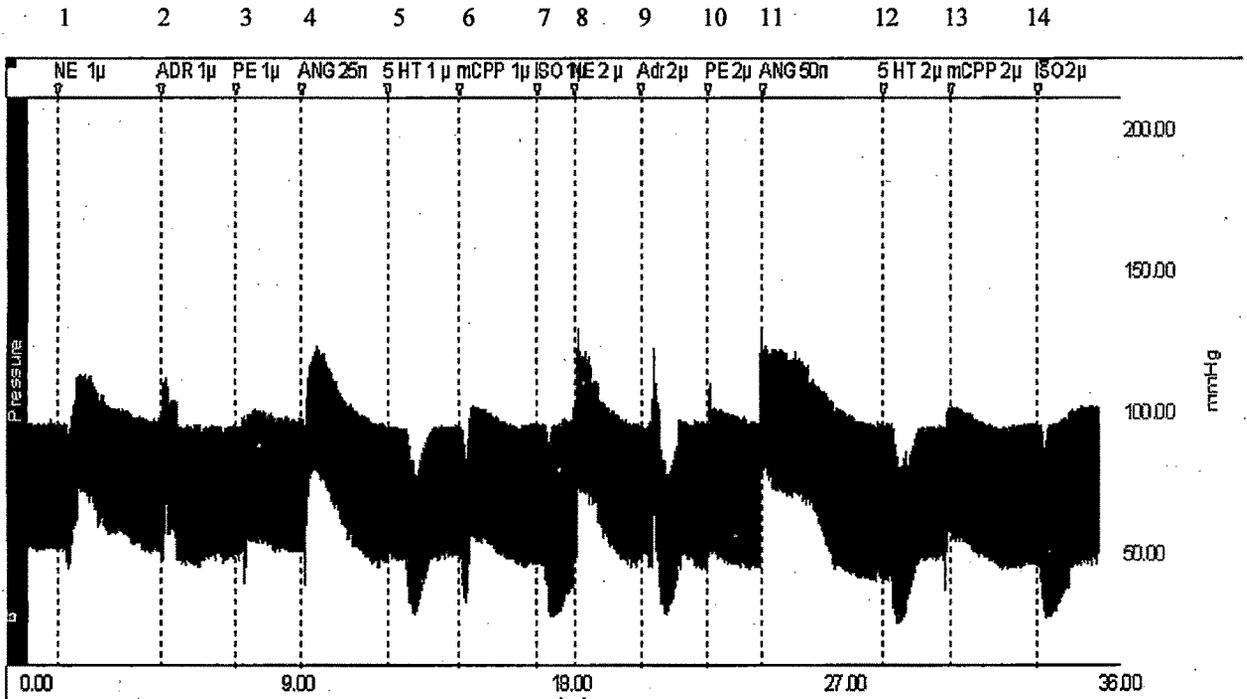
D)



E)



F)



Observation:

- 1) A rise in blood pressure response was noted in (B)- DOCA salt hypertensive rats after [1,8]- noradrenaline (1, 2 μ M/kg, i.v); [2,9]- adrenaline (1, 2 μ M/kg, i.v); and [5,12]- 5-HT (1, 2 μ M/kg, i.v) administration.
- 2) A reduction in blood pressure response was noted in (C)- ME (30 mg/kg) treated DOCA hypertensive rats after [5,12]- 5-HT (1, 2 μ M/kg, i.v) administration.
- 3) A reduction in blood pressure response was noted in (E)- MF (15 mg/kg) treated DOCA hypertensive rats after [5,12]- 5-HT (1, 2 μ M/kg, i.v) administration.

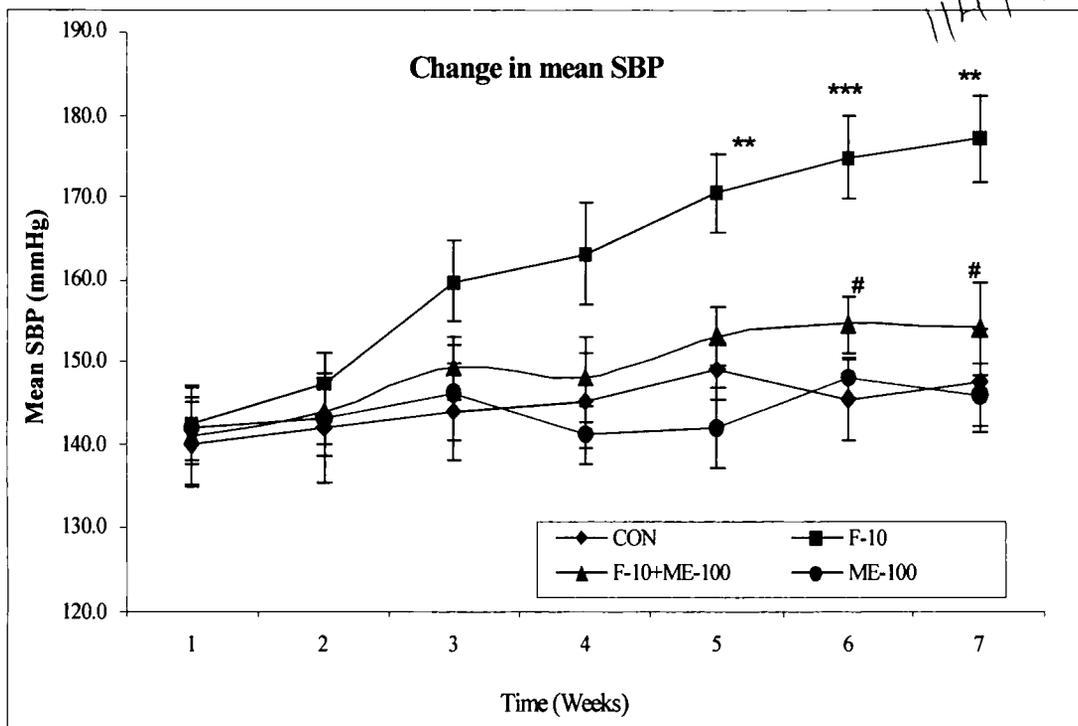


Figure 24: Time course (weekly) changes in Systolic blood pressure (mmHg) during 6 weeks in Control, F-10, F-10+ME-100, ME-100 treated groups. ** $P < 0.01$, *** $P < 0.001$ when compared to control rats. # $P < 0.05$ when compared to fructose hypertensive rats. All values are expressed as mean \pm SEM. Vertical lines represent SEM, $n=6$

SBP- Systolic blood pressure

F-10- Fructose (10% solution)

ME- Methanolic extract of *Trigonella foenum graecum* seeds

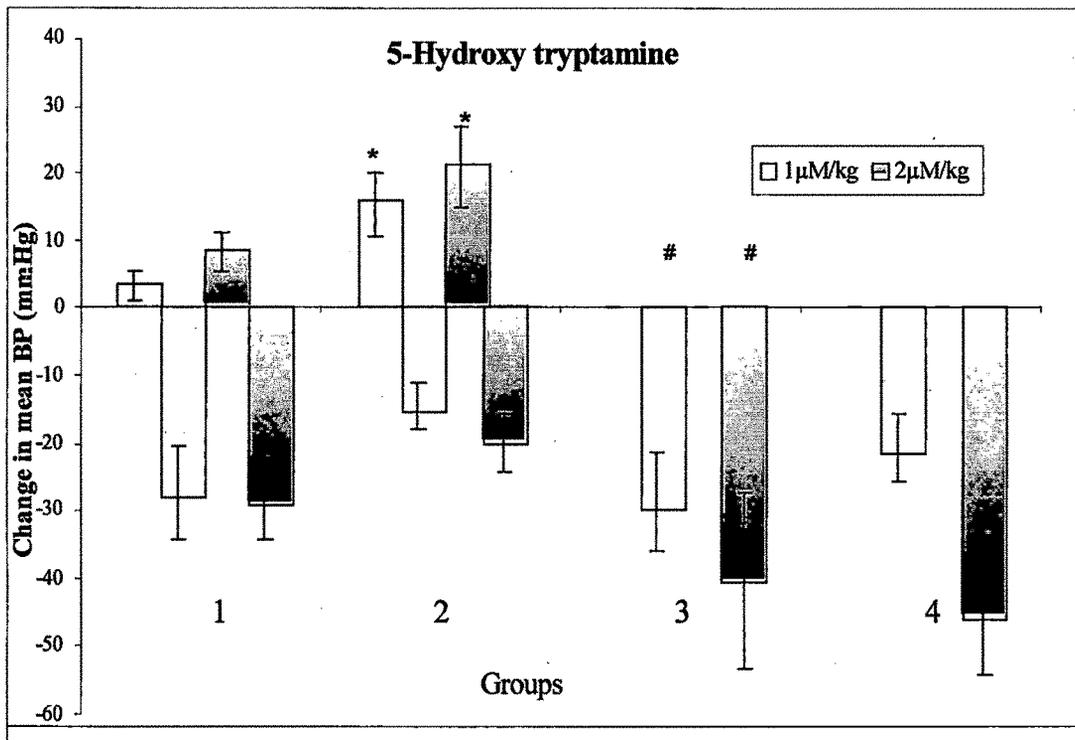


Figure 25a: Change in mean blood pressure to 5-HT (1 μM/kg, i.v; 2 μM/kg, i.v) in (1)- Control, (2)- F-10, (3)- F-10+ME-100, (4)- ME-100 treated groups after completion of 6-week treatment schedule. *P<0.05 when compared to control rats. #P<0.05 when compared to fructose hypertensive rats. All values are expressed as mean ± SEM. Vertical lines represent SEM, n=6

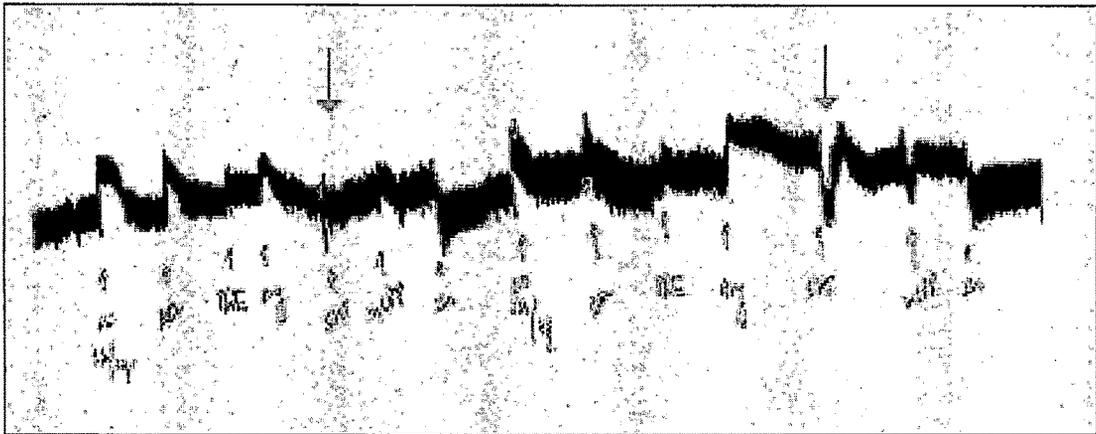
BP- Blood pressure

ME- Methanolic extract of *Trigonella foenum graecum*

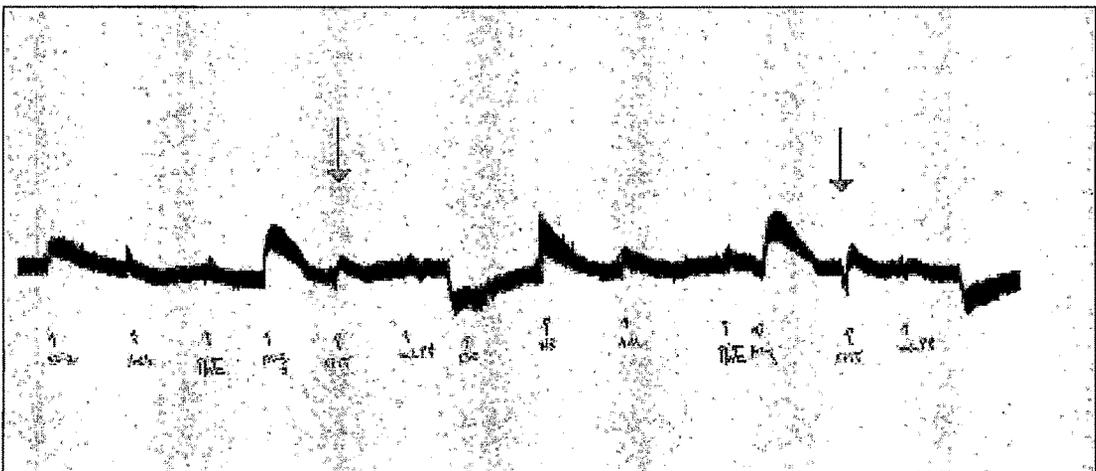
F-10-Fructose (10%)

Tracing 25b: Tracing of arterial blood pressure of anaesthetized rat (urethane 120 mg/100 gm) using UGO Basile–Two Channel blood pressure recorder after intravenous administration of Noradrenaline (1, 2 μ M/kg), Adrenaline (1, 2 μ M/kg), Phenylephrine (1, 2 μ M/kg), 5-Hydroxytryptamine (1, 2 μ M/kg), *m*-CPP (1, 2 μ M/kg), Isoprenaline (1, 2 μ M/kg) and Angiotensin-II (25, 50 nM/kg) of (A) control group, (B) fructose (10%) fed group, (C) ME (100 mg/kg) treated fructose (10%) fed group and (D) ME (100 mg/kg) treated group after completion of 6-week treatment schedule.

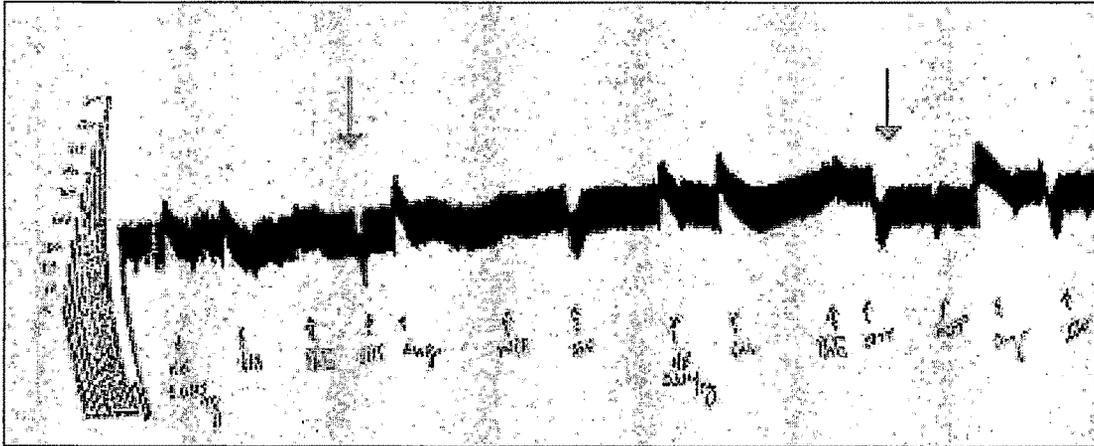
A)



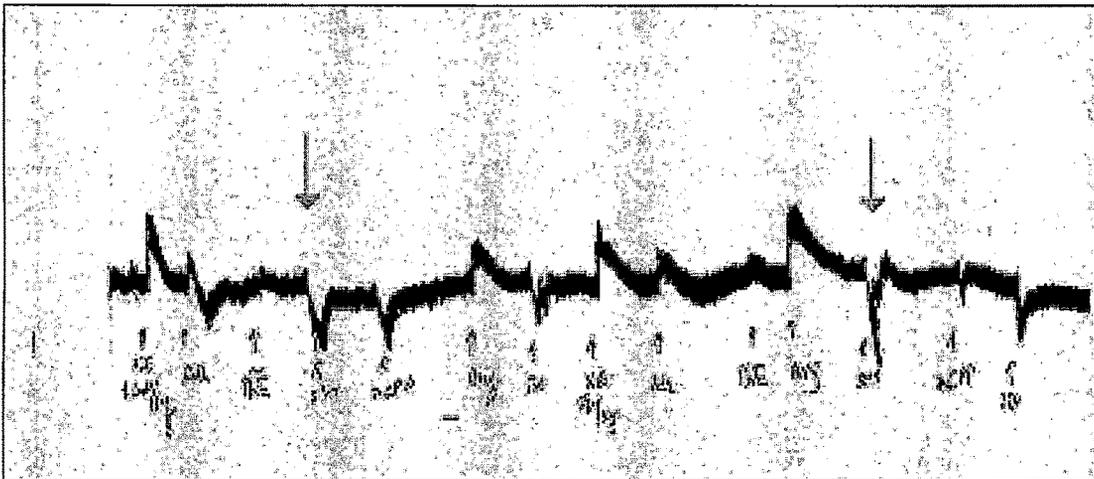
B)



C)



D)



Observation:

- 1) A rise in blood pressure response was noted in (B)- fructose (10%) fed rats after 5-HT (1, 2 μ M/kg, i.v) administration.
- 2) A reduction in blood pressure response was noted in (C) ME (100 mg/kg) treated fructose (10%) fed rats after 5-HT (1, 2 μ M/kg, i.v) administration.

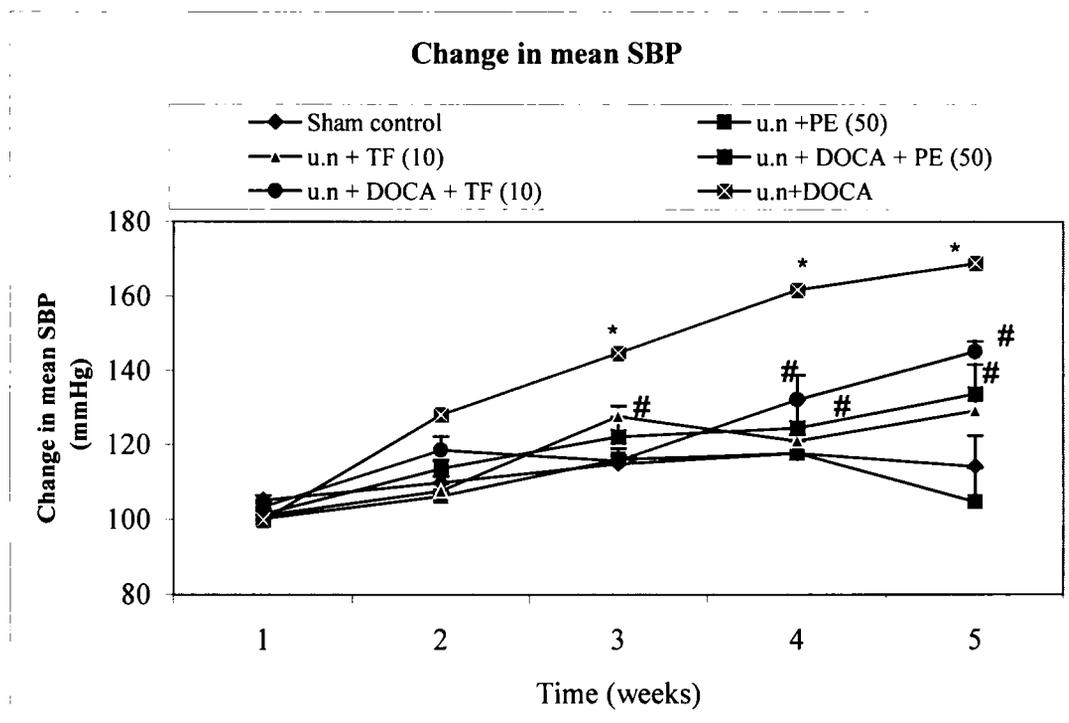


Figure 26: Time course (weekly) of changes in mean arterial pressure (mmHg) during 5 weeks in Sham control, PE-50, TF-10, DOCA, DOCA +PE-50, DOCA +TF-10 treated groups after completion of 4-week treatment schedule. *P<0.05 when compared to sham control group. #P<0.05 when compared to DOCA hypertensive rats. All values are expressed as mean \pm SEM. Vertical lines represent SEM, n=5.

SBP- Systolic Blood Pressure

PE- Pet ether extract of *Zingiber officinale*

TF- Toluene fraction of Petroleum ether extract of *Zingiber officinale*

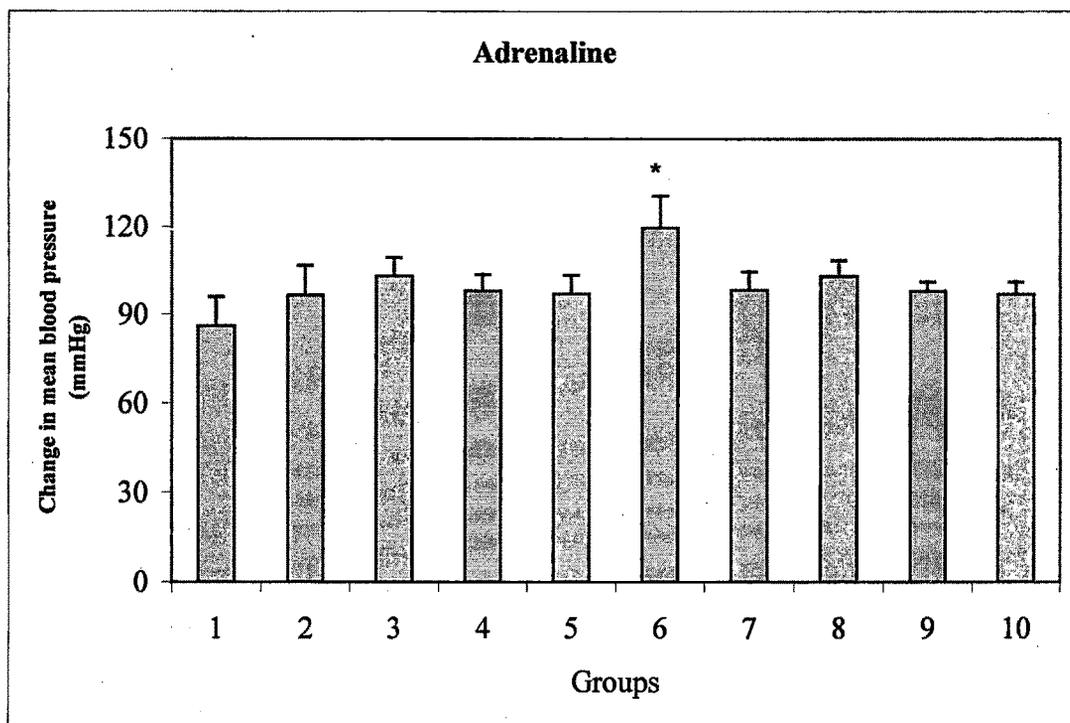


Figure 27: Change in mean blood pressure (mmHg) to Adrenaline (0.5 $\mu\text{g}/\text{kg}$, i.v) in (1)- Sham control, (2)-PE-50, (3)-TF-10, (4)-PPE- 30,(5)- KGE-30, (6)-DOCA, (7)-DOCA +PE-50, (8)-DOCA +TF-10, (9)-DOCA + PPE-30, (10)- DOCA + KGE-30 treated groups after completion of 4-week treatment schedule. * $P < 0.05$ when compared to sham control. All values are expressed as mean \pm SEM. Vertical lines represent SEM, $n=5$.

■ = Rise in blood pressure

PE- Pet ether extract of *Zingiber officinale*

TF- Toluene fraction of Petroleum ether extract of *Zingiber officinale*

PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes;

KGE - Ethanolic extract of *Korean ginseng* roots

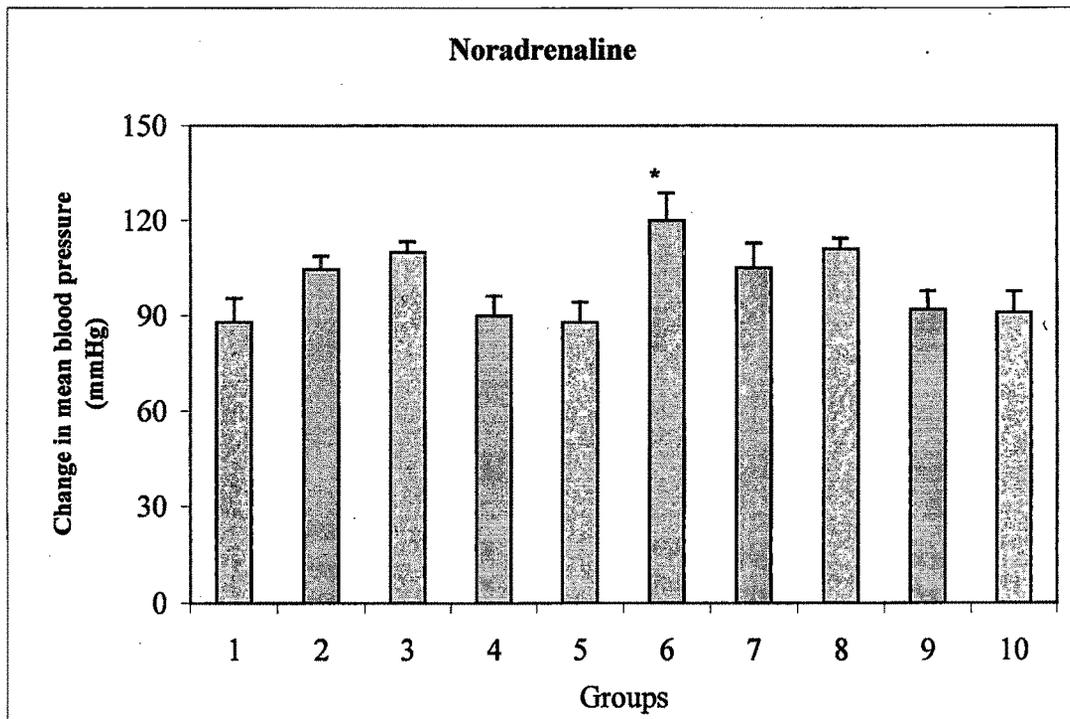


Figure 28: Change in mean blood pressure (mmHg) to Noradrenaline (0.5 µg/kg, i.v) in (1)- Sham control, (2)-PE-50, (3)-TF-10, (4)-PPE- 30,(5)- KGE- 30, (6)-DOCA, (7)-DOCA+PE-50, (8)-DOCA+TF-10, (9)-DOCA+ PPE-30, (10)- DOCA+KGE-30 treated groups after completion of 4-week treatment schedule. *P<0.05 when compared to sham control. All values are expressed as mean ± SEM. Vertical lines represent SEM, n=5.

■ = Rise in blood pressure

PE- Pet ether extract of *Zingiber officinale*

TF- Toluene fraction of Petroleum ether extract of *Zingiber officinale*

PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes;

KGE - Ethanolic extract of *Korean ginseng* roots

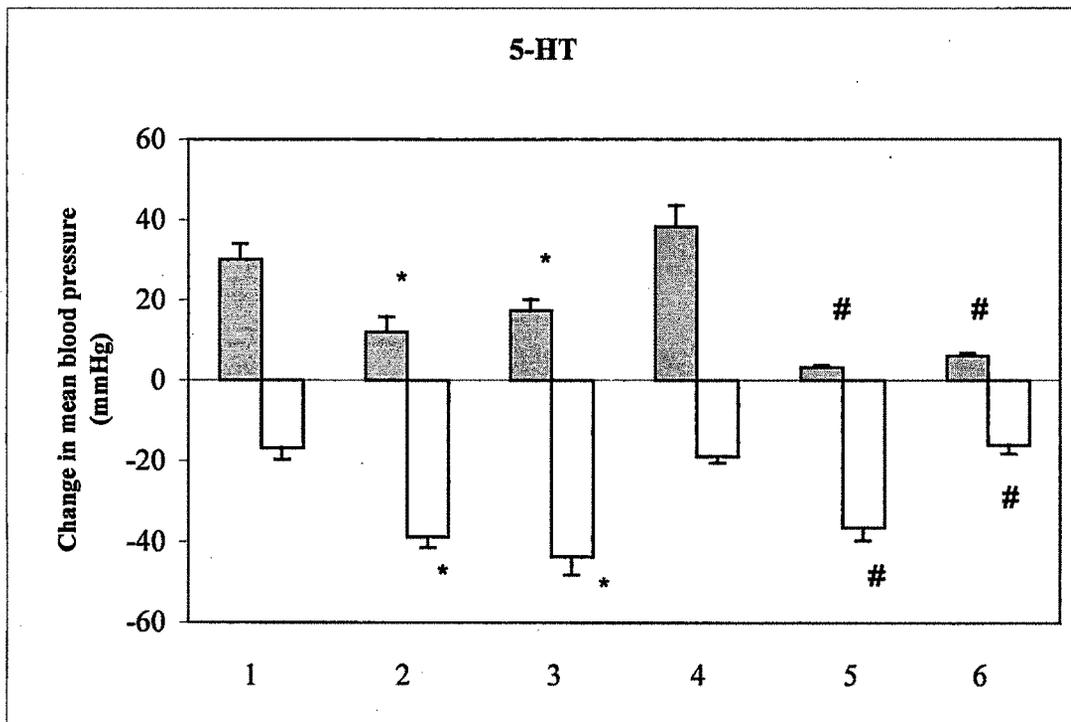


Figure 29a: Change in mean blood pressure (mmHg) to 5-HT (0.5 $\mu\text{g}/\text{kg}$, i.v) in (1)-Sham control, (2)-PE-50, (3)-TF-10, (4)- DOCA, (5)-DOCA +PE-50, (6)-DOCA +TF-10 treated groups after completion of 4-week treatment schedule. * $P < 0.05$ when compared to sham control and # $P < 0.05$ when compared to DOCA hypertensive rats. All values are expressed as mean \pm SEM. Vertical lines represent SEM, $n=5$.

- = Rise in blood pressure
- = Fall in blood pressure

PE- Pet ether extract of *Zingiber officinale*

TF-Toluene fraction of Petroleum ether extract of *Zingiber officinale*

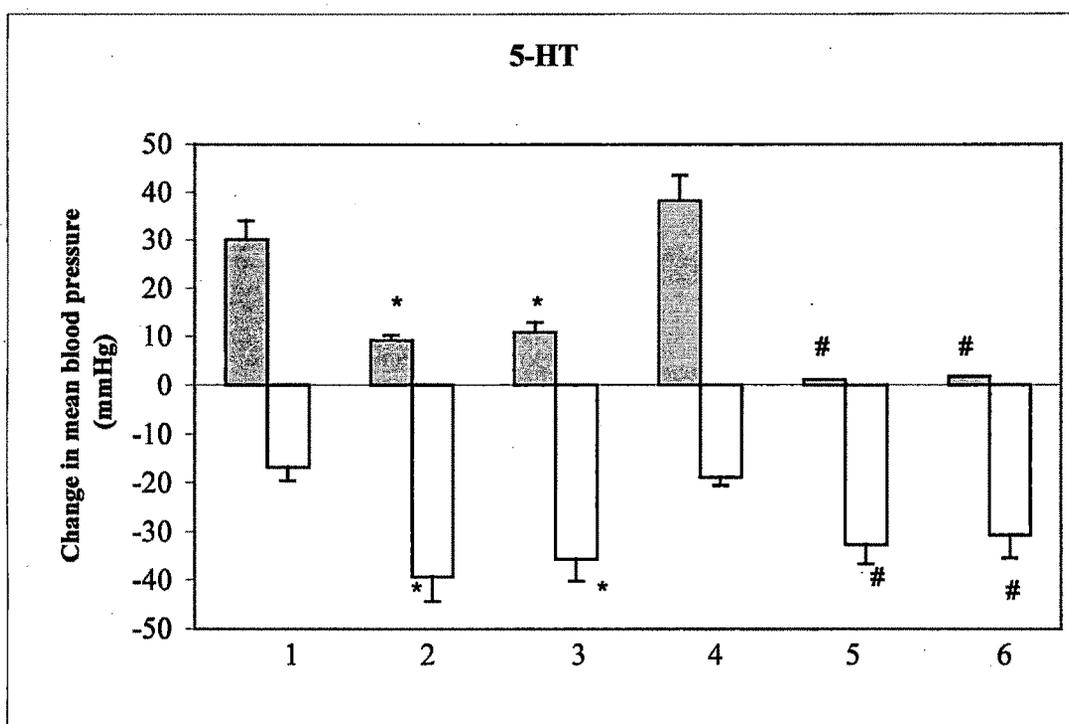


Figure 30a: Change in mean blood pressure (mmHg) to 5-HT (0.5 $\mu\text{g}/\text{kg}$, i.v) in (1)-Sham control, (2)-PPE- 30, (3)-KGE- 30, (4)- DOCA, (5)-DOCA +PPE-30, (6)-DOCA +KGE-30 treated groups after completion of 4-week treatment schedule. * $P < 0.05$ when compared to sham control and # $P < 0.05$ when compared to DOCA hypertensive rats. All values are expressed as mean \pm SEM. Vertical lines represent SEM, $n=5$.

■ = Rise in blood pressure

□ = Fall in blood pressure

PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes;

KGE - Ethanolic extract of *Korean ginseng* roots

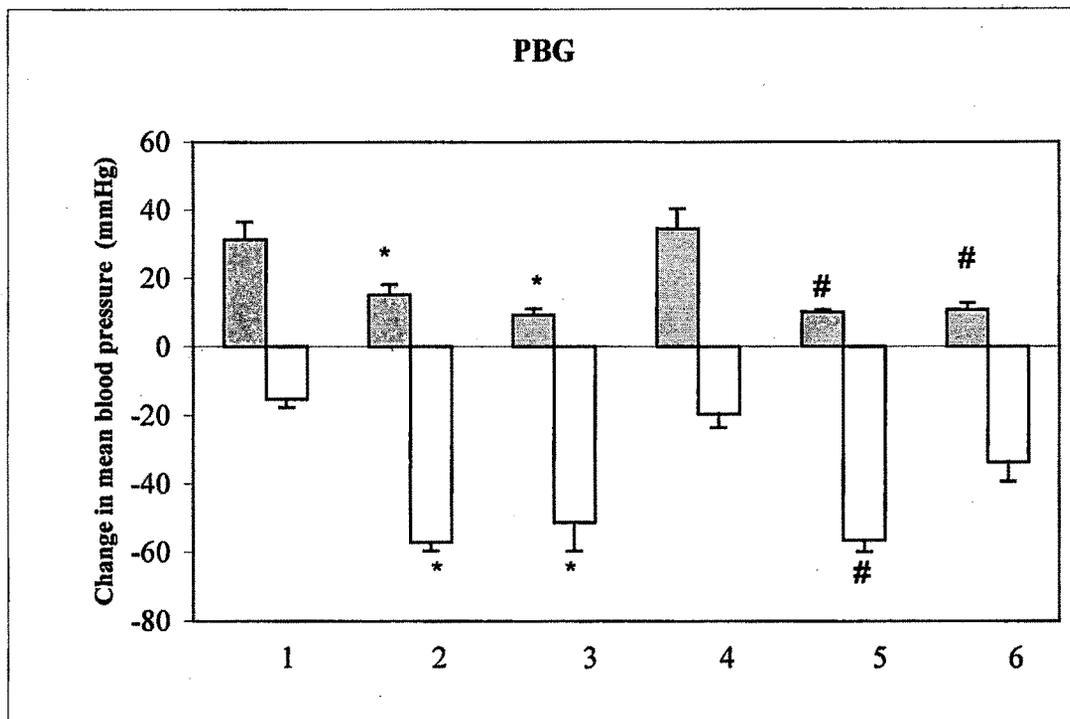


Figure 31a: Change in mean blood pressure (mmHg) to Phenylbiguanide (PBG-0.5 $\mu\text{g}/\text{kg}$, i.v) in (1)-Sham control, (2)-PE-50, (3)-TF-10, (4)- DOCA, (5)- DOCA +PE-50, (6)-DOCA +TF-10 treated groups after completion of 4-week treatment schedule.

* $P < 0.05$ when compared to sham control and # $P < 0.05$ when compared to DOCA hypertensive rats. All values are expressed as mean \pm SEM. Vertical lines represent SEM, $n=5$.

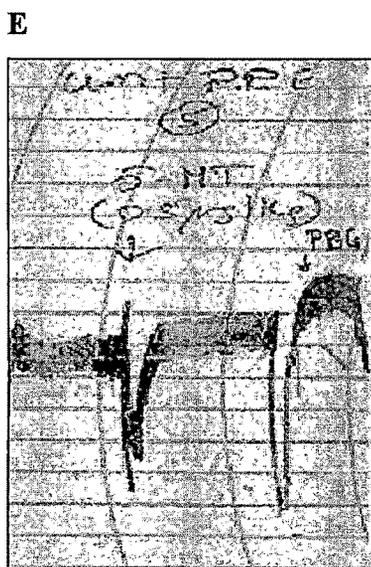
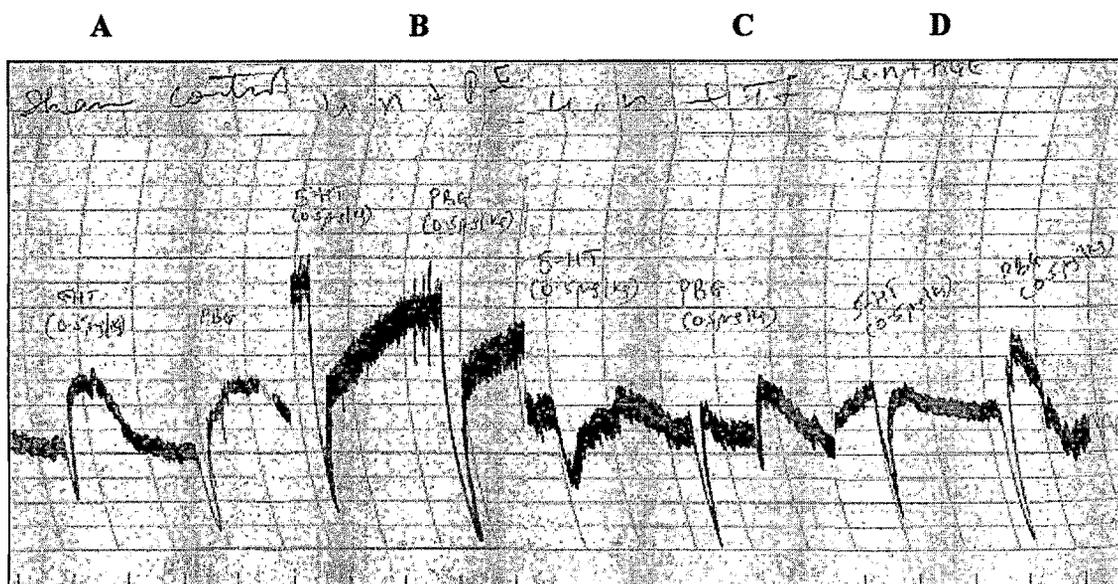
■ = Rise in blood pressure

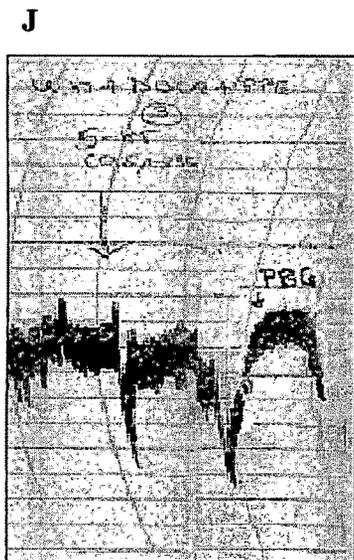
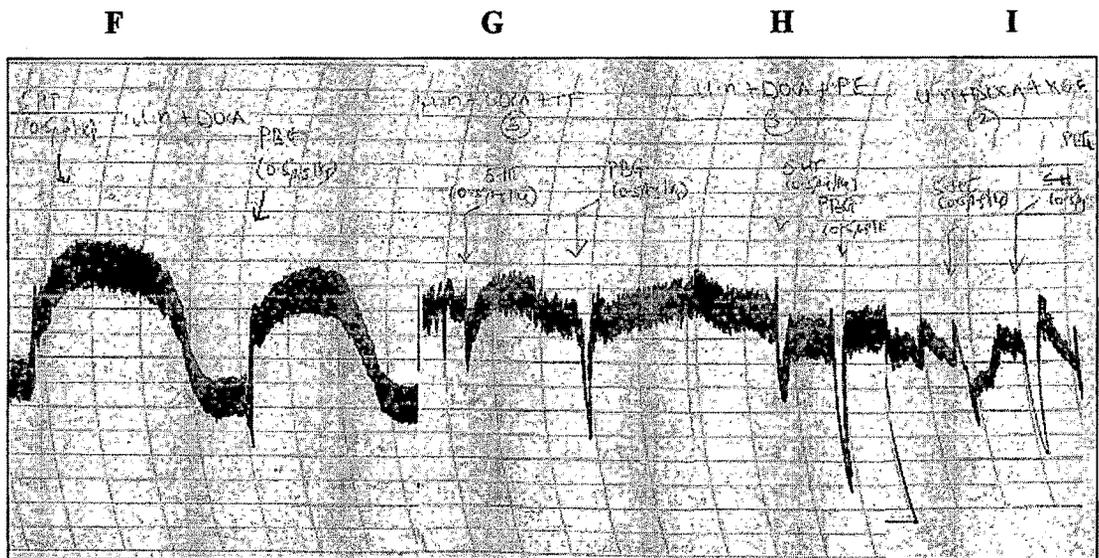
□ = Fall in blood pressure

PE- Pet ether extract of *Zingiber officinale*

TF-Toluene fraction of Petroleum ether extract of *Zingiber officinale*

Tracing 29b, 30b, 31b: Tracing of arterial blood pressure of anaesthetized rat (urethane 120 mg/100 gm) using UGO Basile–Two Channel blood pressure recorder after intravenous administration of 5-HT (0.5 µg/kg), PBG (0.5 µg/kg) in (A) Sham control, (B) U.N + PE, (C) U.N + TF, (D) U.N + KGE, (E) U.N + PPE, (F) U.N + DOCA, (G) U.N + DOCA + TF, (H) U.N + DOCA + PE, (I) U.N + DOCA + KGE, (J) U.N + DOCA + PPE groups after completion of 4-week treatment schedule.





Observation:

- 1) A reduction in blood pressure response was noted in (B) U.N + PE, (C) U.N + TF, (D) U.N + KGE, (E) U.N + PPE, (G) U.N + DOCA + TF, (H) U.N + DOCA + PE, (I) U.N + DOCA + KGE, (J) U.N + DOCA + PPE groups after 5-HT (0.5 μg/kg, i.v.) administration.
- 2) A reduction in blood pressure response was noted in (B) U.N + PE, (C) U.N + TF, (G) U.N + DOCA + TF, (H) U.N + DOCA + PE groups after PBG (0.5 μg/kg, i.v.) administration.

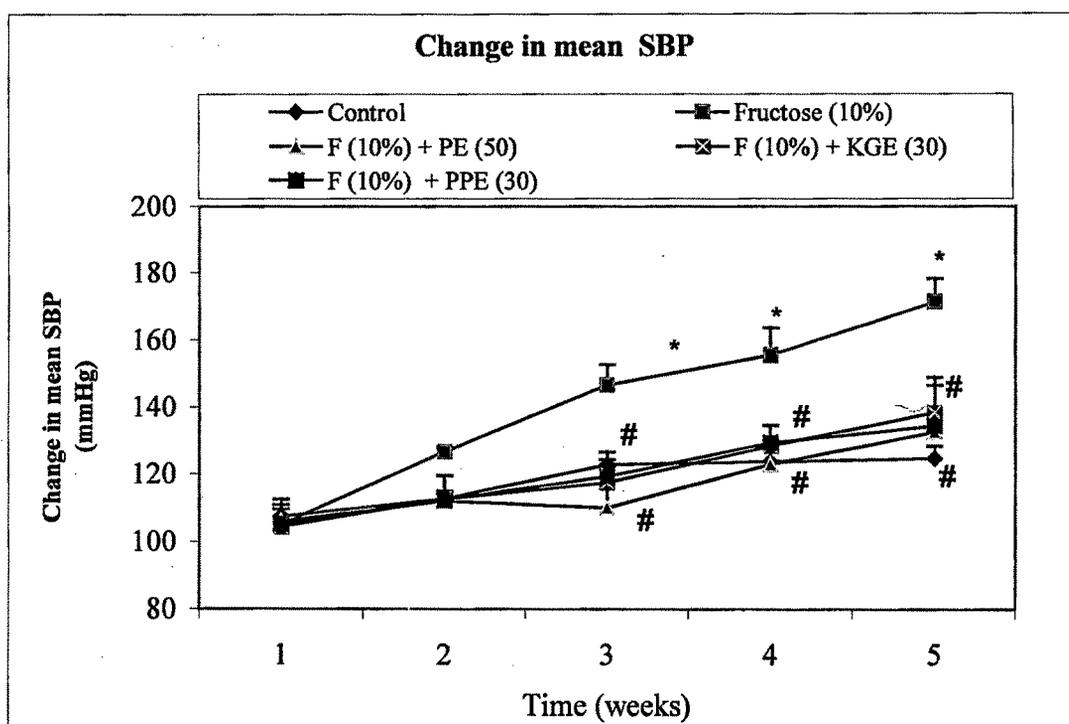


Figure 32: Time course (weekly) of changes in mean arterial pressure (mmHg) during 5 weeks in Control, Fructose (10%), F (10%) +PE-50, F (10%) + PPE- 30, F (10%) + KGE-30 treated groups. *P<0.05 when compared to control group. #P<0.05 when compared to F(10%) rats. Vertical lines represent SEM, n=5.

SBP= Systolic blood pressure

F (10%)= Fructose (10% solution)

PE- Pet ether extract of *Zingiber officinale*

PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes;

KGE - Ethanolic extract of *Korean ginseng* roots

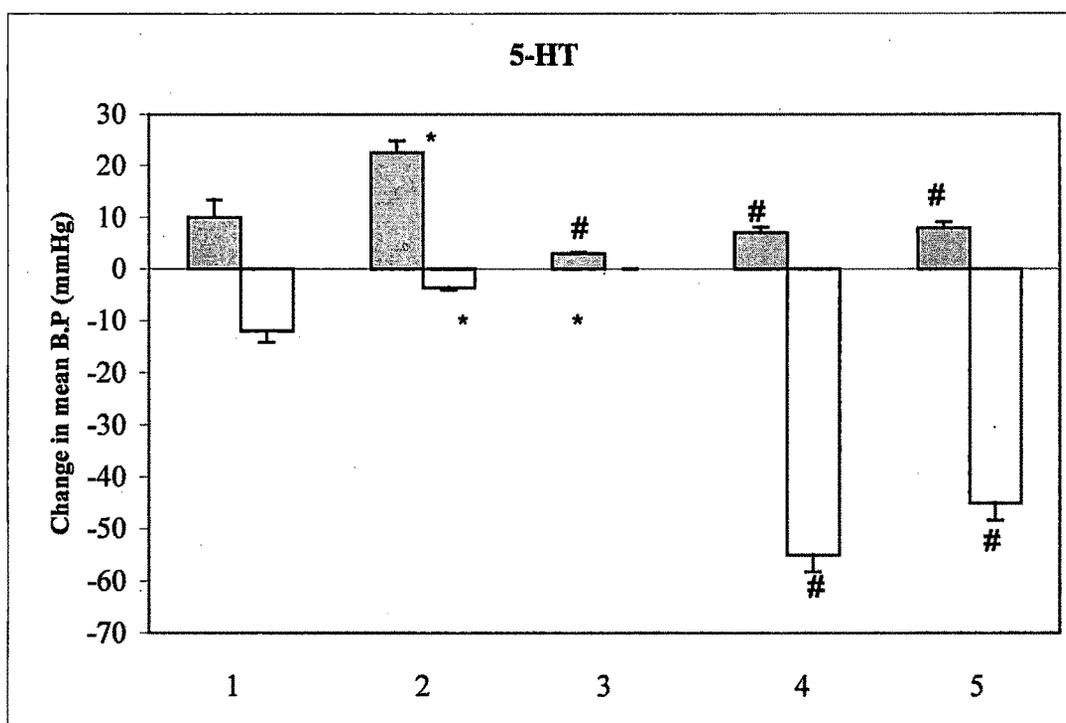


Figure 33a: Change in mean blood pressure to 5-HT (0.5 $\mu\text{g}/\text{kg}$, i.v) in (1)-Control, (2)- Fructose (10%), (3)- F (10%) +PE-50, (4)- F (10%) + PPE- 30, (5)- F (10%) + KGE-30 treated groups after completion of 5-week treatment schedule.* $P < 0.05$ when compared to control group after completion of 5-week treatment schedule. # $P < 0.05$ when compared to F (10%) rats. All values are expressed as mean \pm SEM. Vertical lines represent SEM, $n=5$.

■ = Rise in blood pressure
□ = Fall in blood pressure

B.P- Blood Pressure

PE- Pet ether extract of *Zingiber officinale*

PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes;

KGE - Ethanolic extract of *Korean ginseng* roots

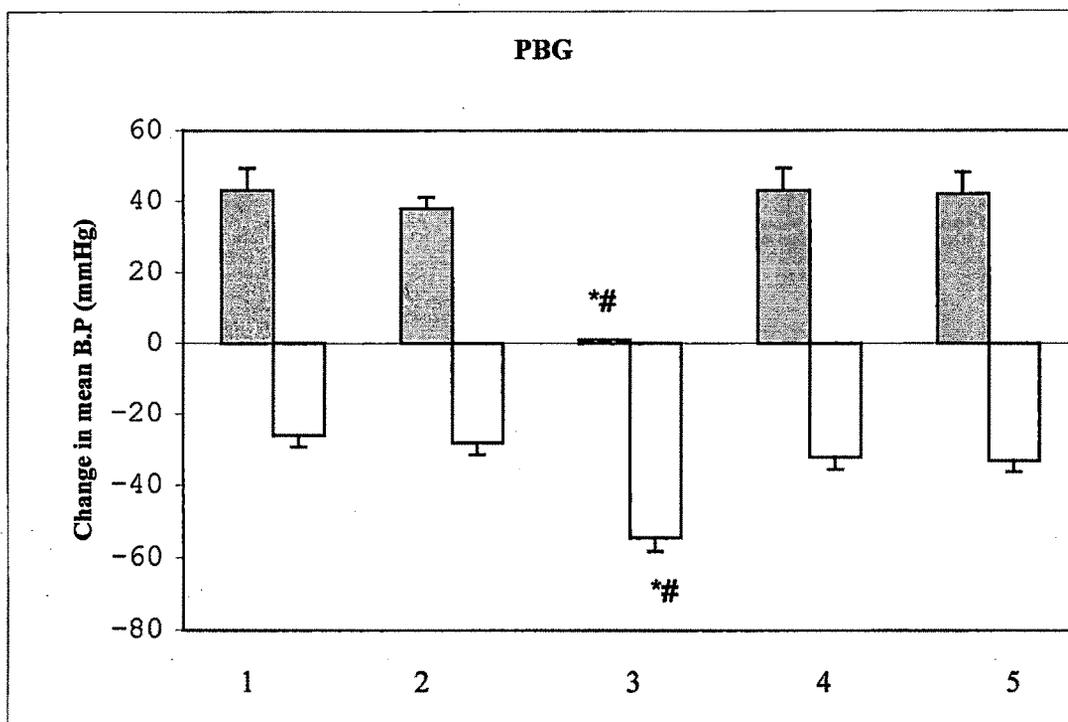


Figure 34a: Change in mean blood pressure (mmHg) to Phenylbiguanide (PBG- 0.5 μ g/kg, i.v) in (1)- Control, (2)- Fructose (10%), (3)- F (10%) +PE-50, (4)- F (10%) + PPE-30, (5)- F (10%) + KGE-30 treated groups after completion of 5-week treatment schedule. *P<0.05 when compared to control group. #P<0.05 when compared to F (10%) rats. All values are expressed as mean \pm SEM. Vertical lines represent SEM, n=5.

- = Rise in blood pressure
- = Fall in blood pressure

B.P- Blood pressure

PE-Pet ether extract of *Zingiber officinale*

PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes;

KGE - Ethanolic extract of *Korean ginseng* roots

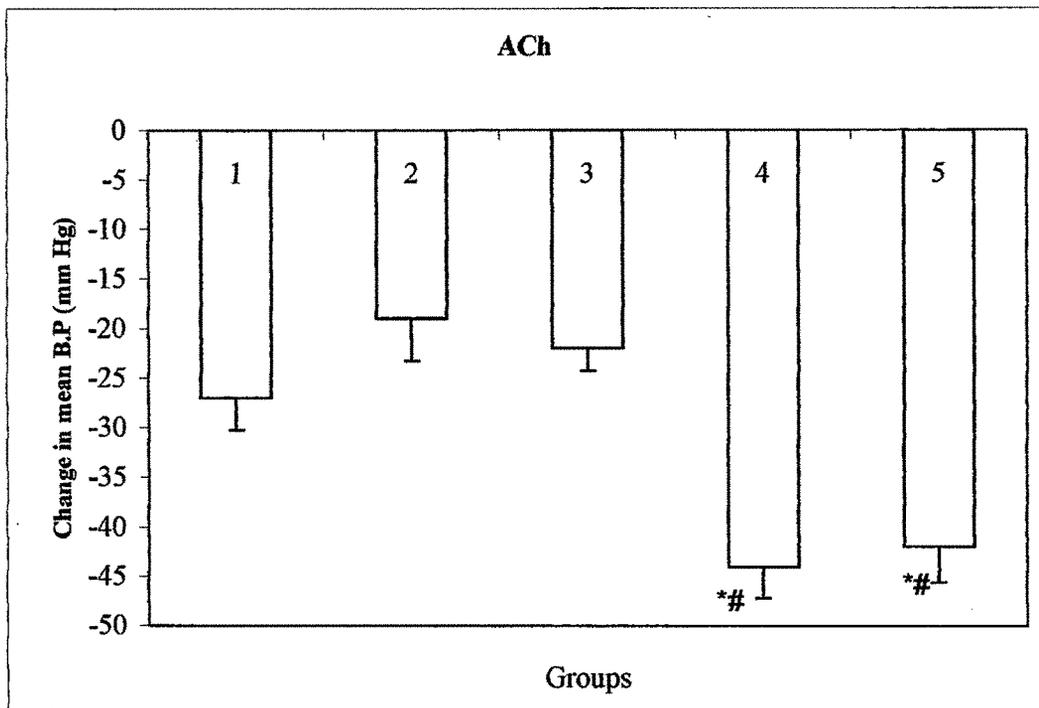


Figure 35a: Mean change in blood pressure (mmHg) to Acetylcholine (ACh-0.5µg/kg, i.v) in (1)- Control, (2)- Fructose (10%), (3)- F (10%) +PE-50, (4)- F (10%) + PPE- 30, (5)- F (10%) + KGE-30 treated groups after completion of 5-week treatment schedule. *P<0.05 when compared to control group. #P<0.05 when compared to F (10%) rats. All values are expressed as mean ± SEM. Vertical lines represent SEM, n=5.

□ = Fall in blood pressure

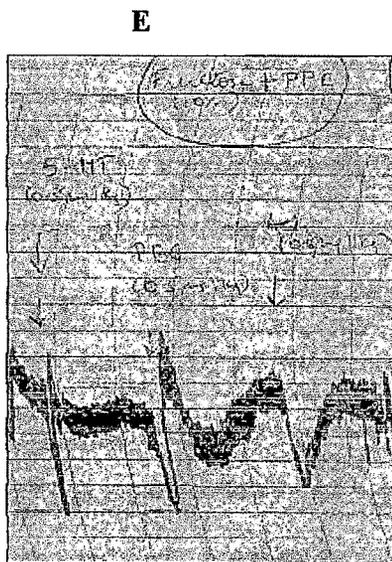
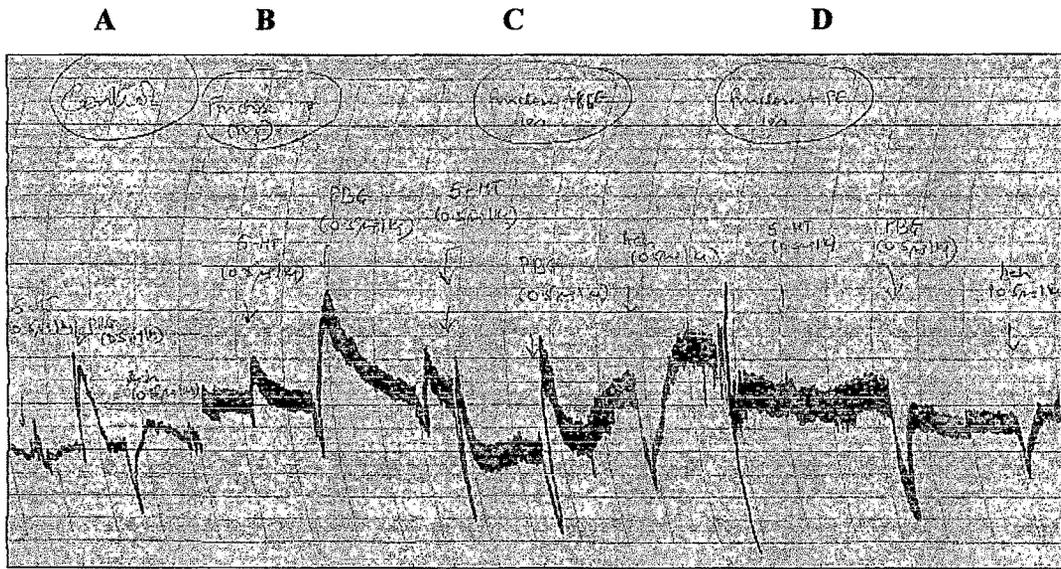
BP- Blood Pressure

PE- Pet ether extract of *Zingiber officinale*

PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes;

KGE - Ethanolic extract of *Korean ginseng* roots

Tracing 33b, 34b, 35b: Tracing of arterial blood pressure of anaesthetized rat (urethane 120 mg/100 gm) using UGO Basile–Two Channel blood pressure recorder after intravenous administration of 5-HT (0.5µg/kg), PBG (0.5 µg/kg), ACh (0.5 µg/kg), of (A) control group, (B) fructose (10%) group, (C) fructose (10%) +KGE (30 mg/kg) group (D) fructose (10%) + PE (50 mg/kg) and (E) fructose (10%) + PPE (30 mg/kg) treated group after completion of 5-week treatment schedule.



Observation:

- 1) A reduction in blood pressure response was noted in (C) fructose (10%) +KGE (30 mg/kg) group (D) fructose (10%) + PE (50 mg/kg) and (E) fructose (10%) + PPE (30 mg/kg) treated group after after 5-HT (0.5 µg/kg, i.v.) administration
- 2) A reduction in blood pressure response was noted in (D) fructose (10%) + PE (50 mg/kg) treated group after after PBG (0.5 µg/kg, i.v.) administration
- 3) A reduction in blood pressure response was noted in (C) fructose (10%) +KGE (30 mg/kg) group and (E) fructose (10%) + PPE (30 mg/kg) treated group after ACh (0.5 µg/kg, i.v.) administration

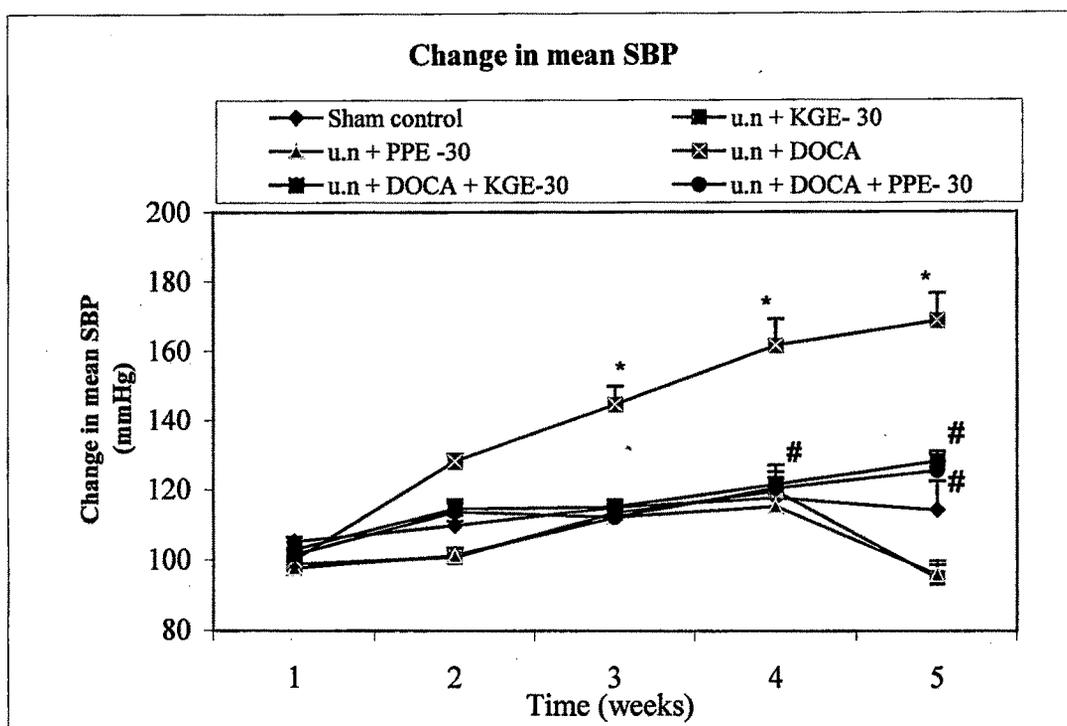


Figure 36: Time course (weekly) of changes in mean arterial pressure (mmHg) during 5 weeks in Sham control, KGE- 30, PPE- 30, DOCA, DOCA + PPE-30, DOCA + KGE- 30 treated groups after completion of 4-week treatment schedule. *P<0.05 when compared to sham control group. #P<0.05 when compared to DOCA hypertensive rats. All values are expressed as mean \pm SEM. Vertical lines represent SEM, n=5.

SBP-Systolic Blood Pressure

PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes;

KGE - Ethanolic extract of *Korean ginseng* roots

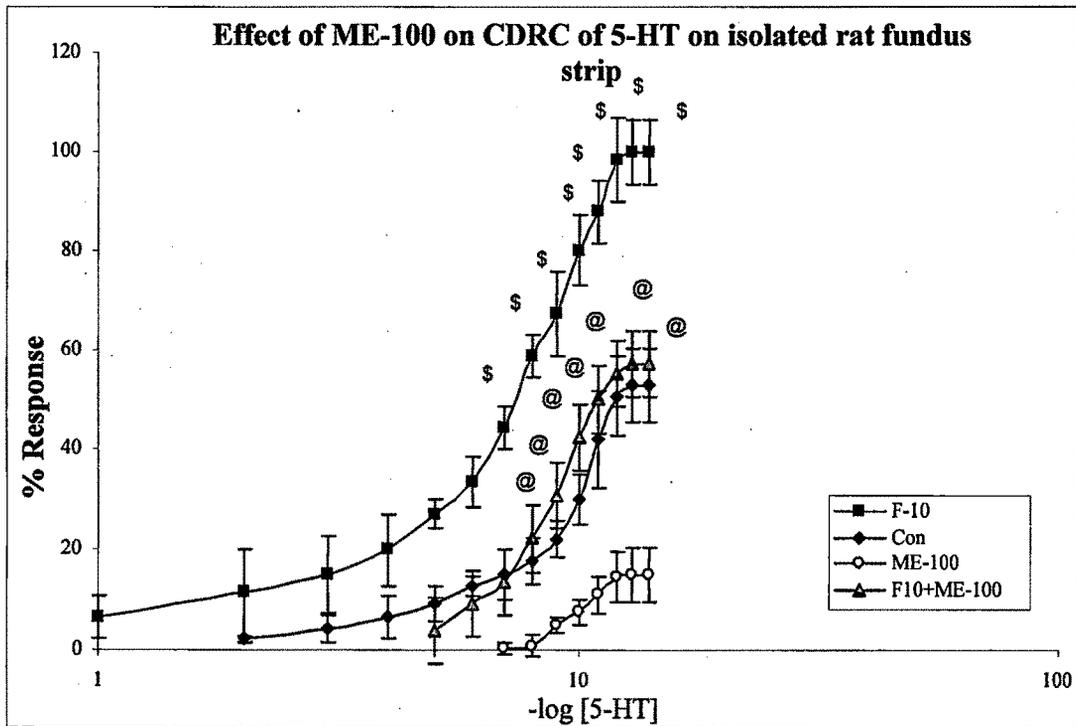


Fig. 37a: Effect of ME-100 on CDRC of 5-HT on isolated rat fundus strip in Control, F-10, F-10+ME-100, and ME-100 after completion of 6- week treatment schedule.

\$P<0.001 when compared to control rats. @P<0.001 when compared to fructose hypertensive rats. All values are expressed as mean \pm SEM. Vertical lines represent SEM, n=6.

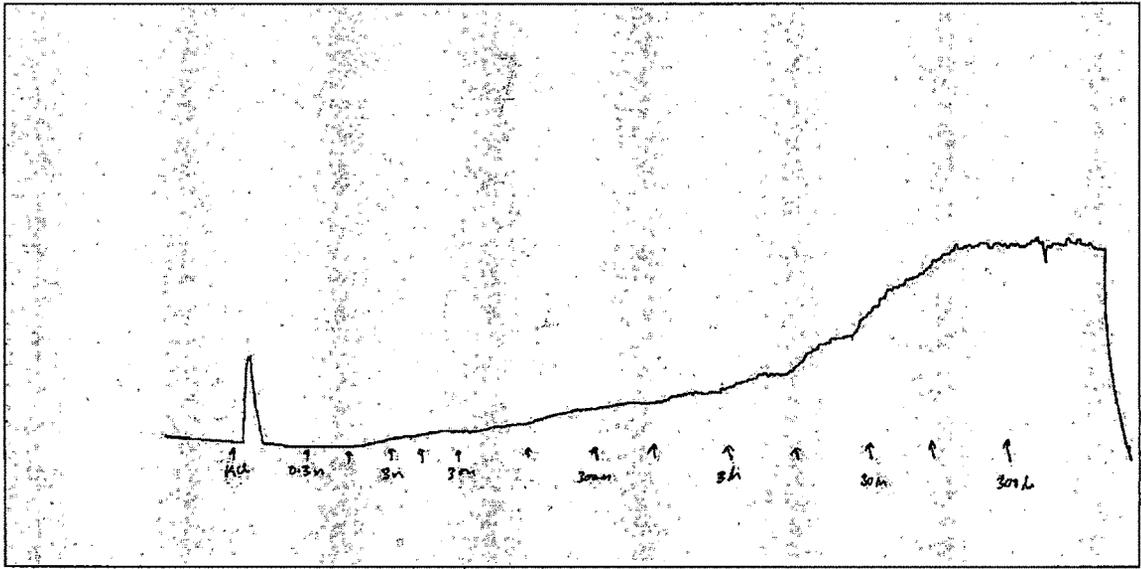
CDRC- Concentration dose response curve

F-10- Fructose (10% solution)

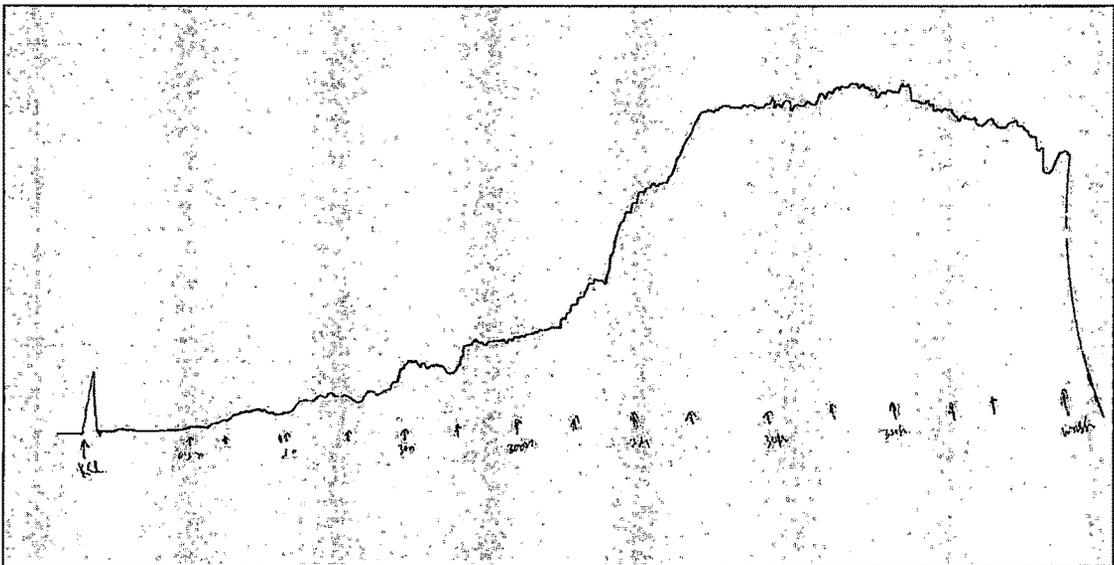
ME- Methanolic extract of *Trigonella foenum graecum* seeds

Tracing 37b: Tracing of Cumulative dose response curve (CDRC) of 5-HT on isolated rat stomach fundus strip using UGO BASILE-Two Channel recorder in A) control rats B) fructose hypertensive rats C) ME-100+fructose rats and D) ME-100 after completion of 6-week treatment schedule.

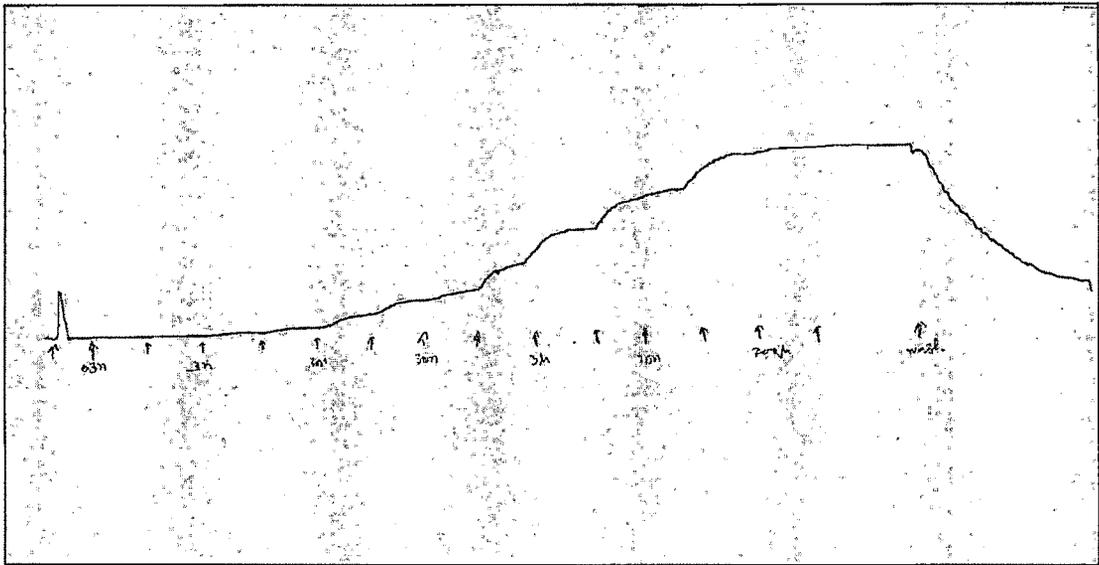
A)



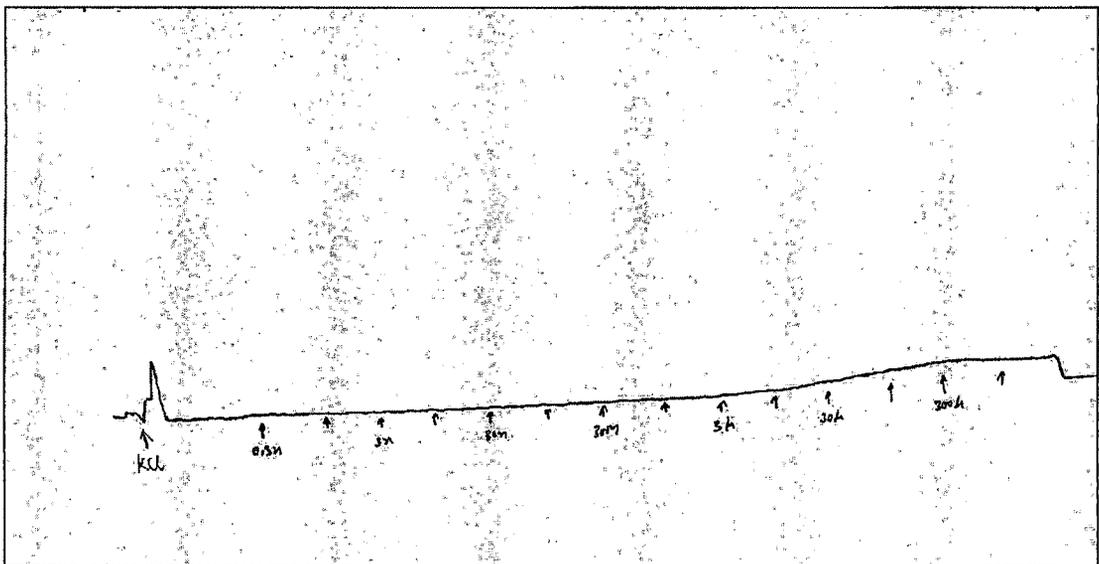
B)



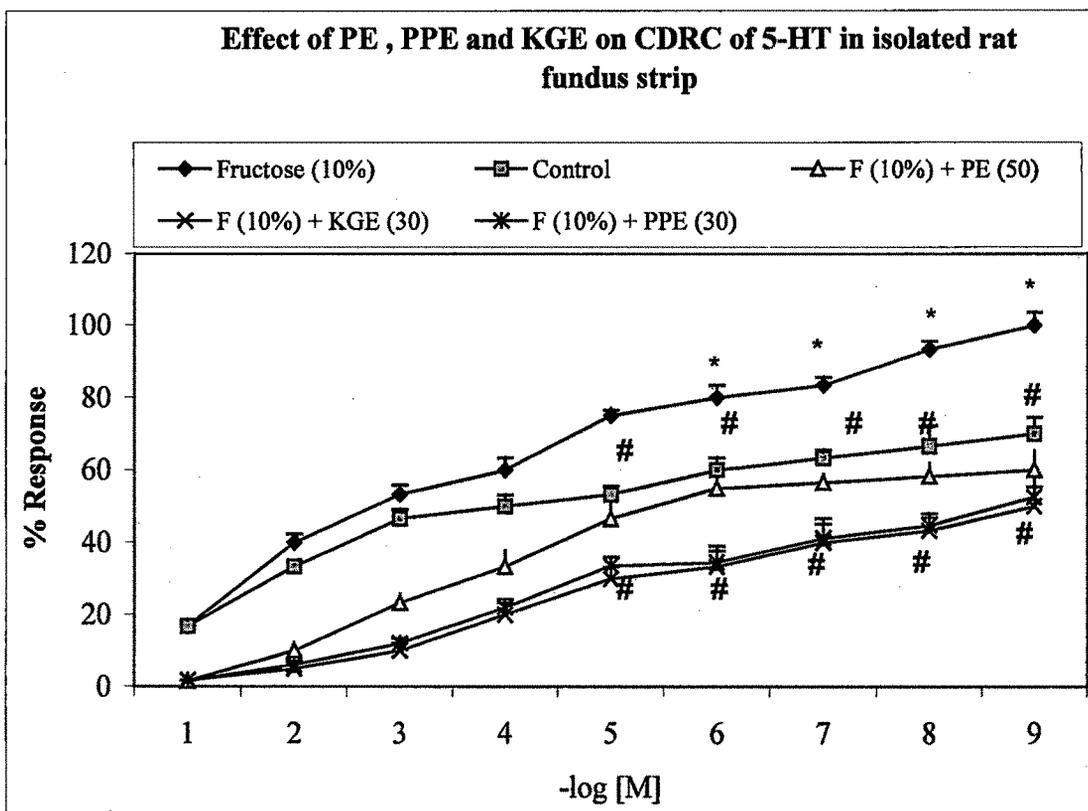
C)



D)



Observation: Suppression of CDRC of 5-HT using rat fundus strip in C) ME-100 + fructose rats and D) ME-100 groups



1= 10.88, 2=10.51, 3= 10.25, 4= 10.04, 5= 9.7, 6= 9.55, 7= 9.26, 8= 8.95, 9= 8.65

Figure 38a: Effect of PE-50, PPE-30 and KGE-30 on CDRC of 5-HT on isolated rat fundus strip in Control, Fructose (10%), F (10%) +PE-50, F (10%) + KGE- 30, F (10%) + PPE- 30 treated groups after completion of 5-week treatment schedule. *P<0.05 when compared to control group. #P<0.05 when compared to F (10%) rats. All values are expressed as mean \pm SEM. Vertical lines represent SEM, n=5.

CDRC- Cumulative dose response curve

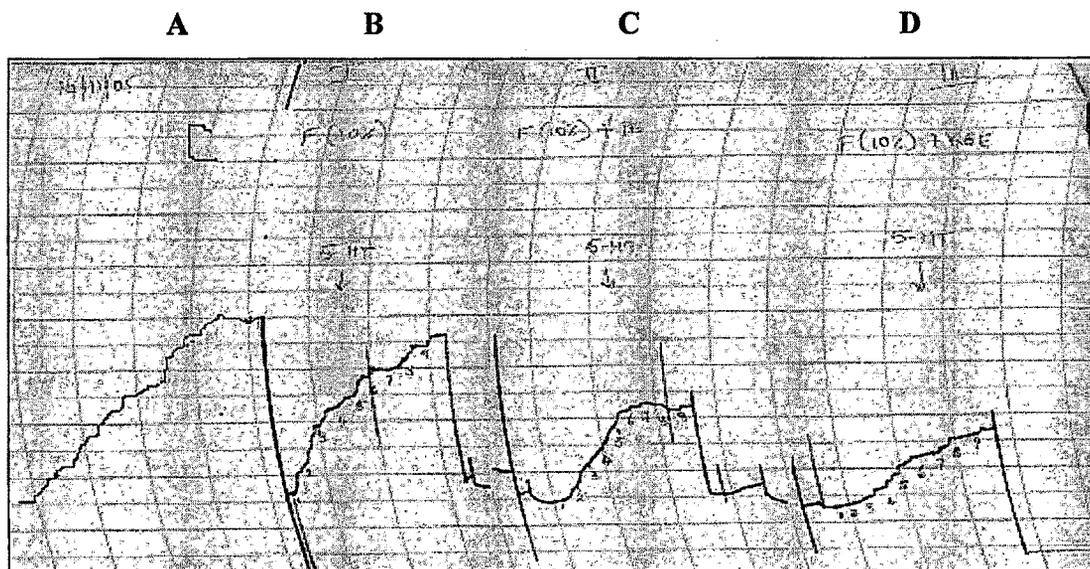
F-Fructose

PE- Pet ether extract of *Zingiber officinale*

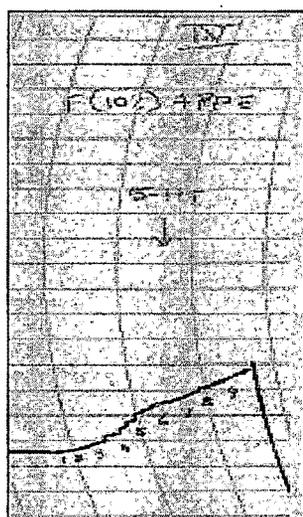
PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes;

KGE - Ethanolic extract of *Korean ginseng* roots

Tracing 38b: Tracing of Cumulative dose response curve (CDRC) of 5-HT on isolated rat fundus strip using UGO BASILE- Two Channel recorder in (A) Control, (B) Fructose (10%), (C) F (10%) +PE-50, (D) F (10%) + KGE- 30, (E) F (10%) + PPE treated groups after completion of 5-week treatment schedule.



E



Observation: Suppression of CDRC of 5-HT using rat fundus strip in C) F (10%) +PE-50, (D) F (10%) + KGE- 30, (E) F (10%) + PPE- 30 groups.

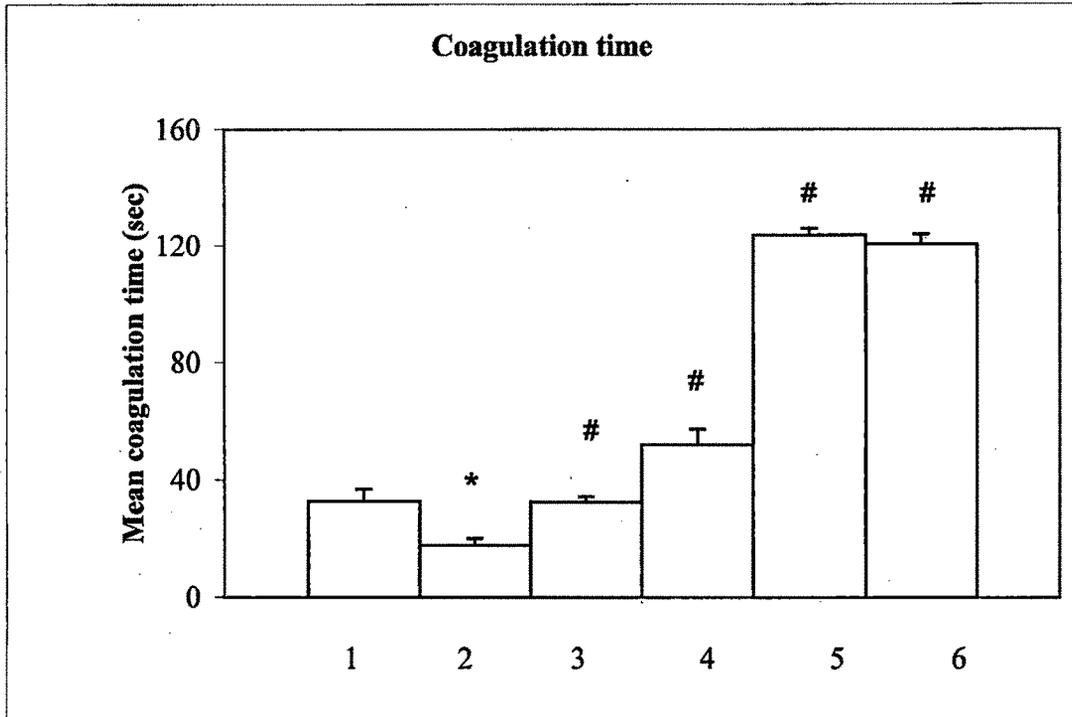


Figure 39: Change in mean blood coagulation time (sec) in (1)- Control, (2)- F-10, (3)- F-10+ME-100, (4)- F-10+PE-50, (5)- F-10+KGE-30, (6)- F-10+PPE-30 after completion of 5-week treatment schedule in Fructose hypertension model. *P<0.05 when compared to control rats; #P<0.05 when compared to fructose hypertensive rats. All values are expressed as mean \pm SEM. Vertical lines represent SEM, n=5.

F-10= Fructose (10%)

ME- Methanolic extract of *Trigonella foenum graecum* seeds

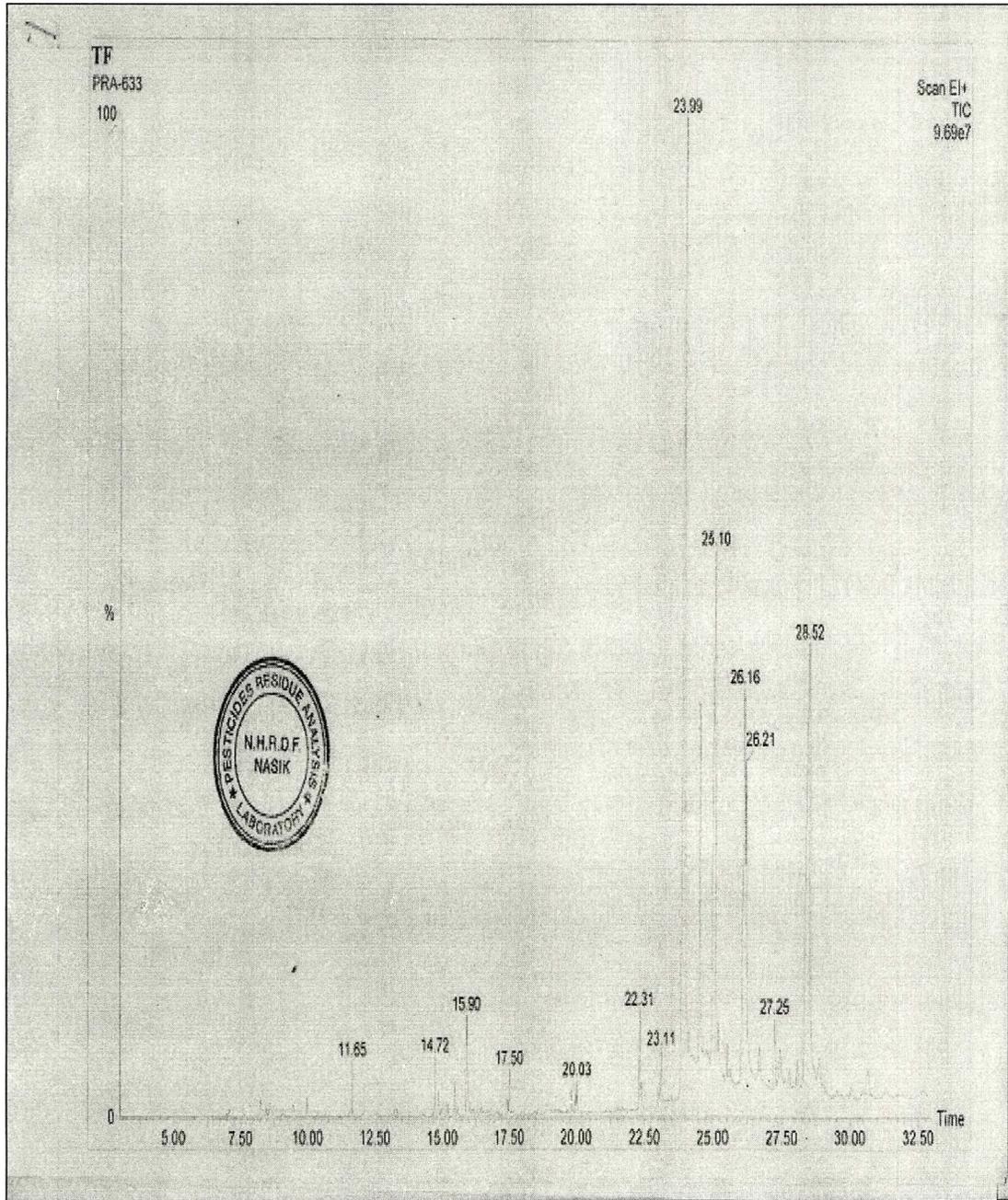
PE- Pet ether extract of *Zingiber officinale*

PPE - n-butanol fraction of ethanol extract of *Panax pseudoginseng* rhizomes

KGE - Ethanolic extract of *Korean ginseng* roots

Figure: 40

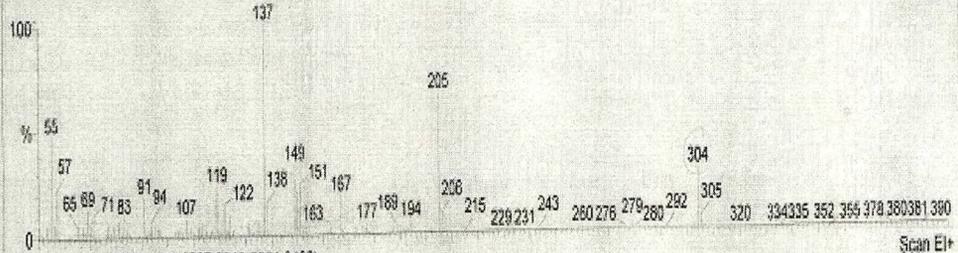
GC-MS Chromatogram of TF



TF

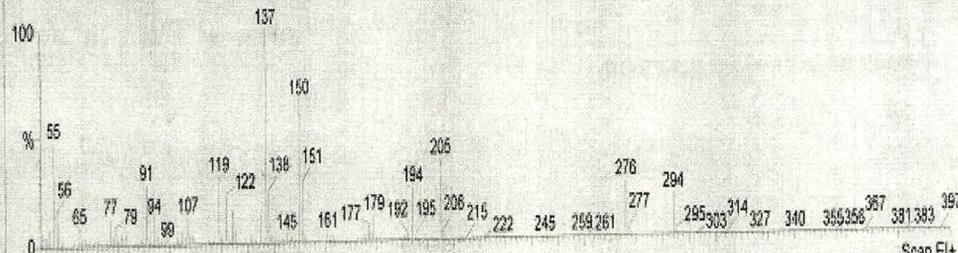
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Scan El+
3.62e6



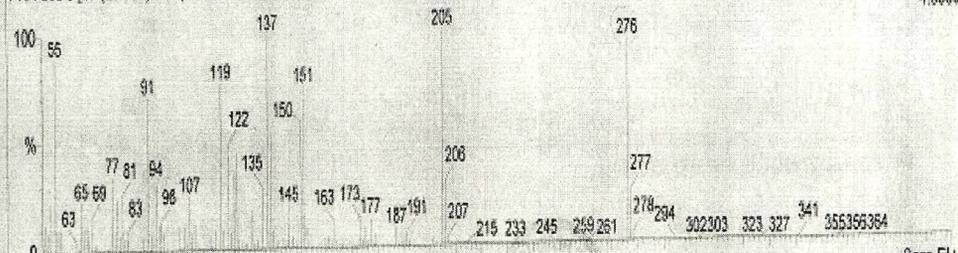
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4.16e6



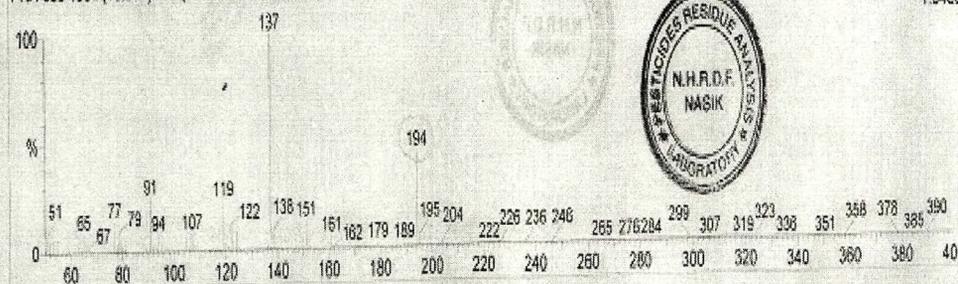
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Scan El+
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PRA-633 1934 (15.896) Cm (1932:1938-1966:2000)

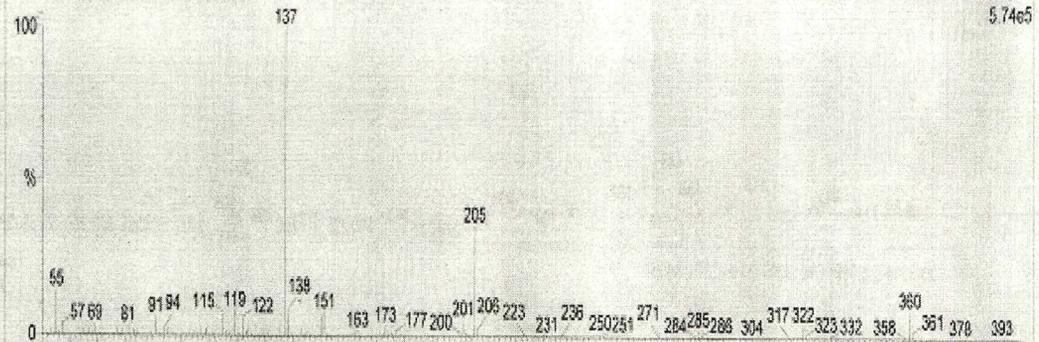
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TF

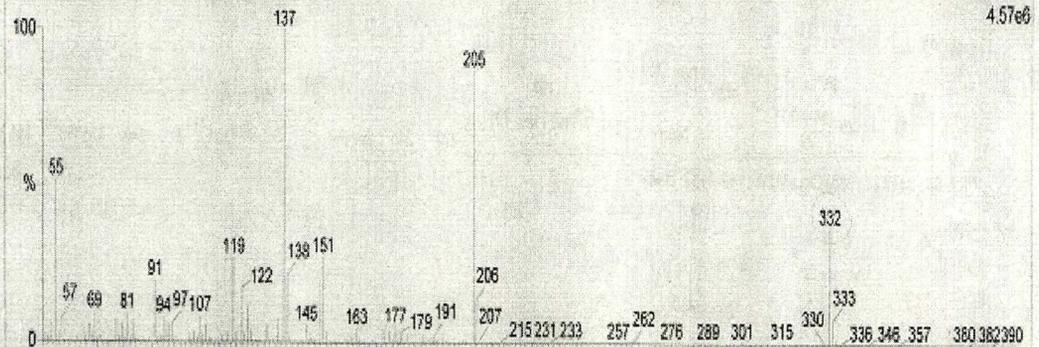
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Scan E1+
5.74e5



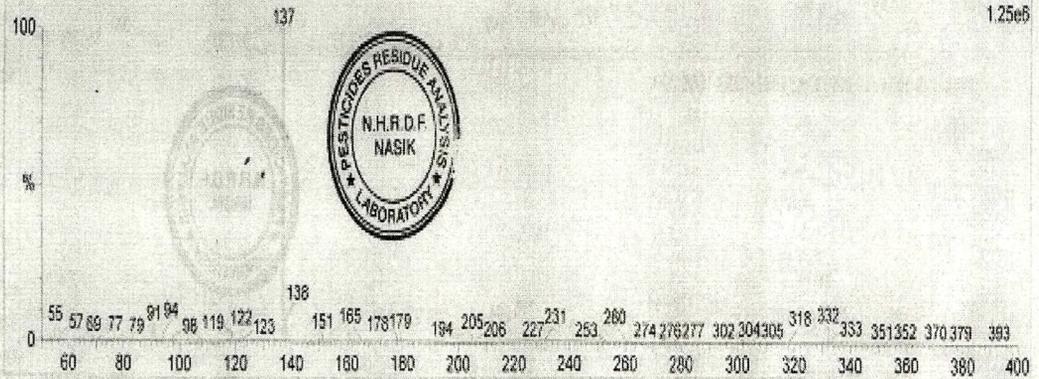
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Scan E1+
4.57e6



PRA-633 3554 (27.434) Cm (3659:3669-3695:3703)

Scan E1+
1.25e6



Area Percent Report

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 Printed : Wednesday, February 23, 2005 4:11:59 PM

#	Name	RT	Area	Height	BL	Conc	Units	Area/Conc	m/z	Area %
1		8.241	85,349.6	1,154,266	bb	0.00		0.00	TIC	24
2		8.608	74,482.8	911,184	bb	0.00		0.00	TIC	21
3		9.455	90,622.3	998,271	bb	0.00		0.00	TIC	26
4		9.981	54,947.9	1,131,930	bb	0.00		0.00	TIC	16
5		11.642	161,745.4	3,263,378	bb	0.00		0.00	TIC	46
6		14.722	160,955.9	3,321,901	bb	0.00		0.00	TIC	46
7		14.862	72,594.0	1,477,599	bb	0.00		0.00	TIC	21
8		15.463	96,913.5	1,952,444	bb	0.00		0.00	TIC	27
9		15.903	532,805.2	6,934,569	bb	0.00		0.00	TIC	1.51
10		17.503	113,855.0	2,481,159	bb	0.00		0.00	TIC	32
11		18.943	81,733.0	510,876	bb	0.00		0.00	TIC	23
12		19.811	75,465.4	1,435,141	bb	0.00		0.00	TIC	21
13		20.030	165,774.4	2,055,638	bb	0.00		0.00	TIC	47
14		22.311	478,588.7	6,573,994	bb	0.00		0.00	TIC	1.35
15		23.025	60,645.5	980,168	bd	0.00		0.00	TIC	17
16		23.112	224,273.4	3,668,608	db	0.00		0.00	TIC	63
17		23.972	9,328,190.0	85,912,320	bd	0.00		0.00	TIC	26.39
18		24.139	504,326.4	3,817,041	db	0.00		0.00	TIC	1.43
19		24.532	1,739,562.5	26,351,932	bd	0.00		0.00	TIC	4.92
20		24.759	147,334.4	1,151,696	db	0.00		0.00	TIC	42
21		25.079	4,704,362.0	43,893,176	bd	0.00		0.00	TIC	13.31
22		25.200	197,065.1	3,028,536	db	0.00		0.00	TIC	56
23		25.526	168,203.2	2,720,543	bd	0.00		0.00	TIC	48
24		25.633	96,124.7	1,191,397	db	0.00		0.00	TIC	27
25		26.146	5,610,791.0	34,499,064	bd	0.00		0.00	TIC	15.87
26		26.687	444,226.3	3,648,896	dd	0.00		0.00	TIC	1.26
27		26.854	123,979.5	905,362	db	0.00		0.00	TIC	35
28		27.241	405,672.2	5,712,288	bb	0.00		0.00	TIC	1.14
29		27.434	256,541.8	2,932,980	bb	0.00		0.00	TIC	73
30		27.781	* 113,080.5	1,478,174	bb	0.00		0.00	TIC	32
31		28.061	208,629.0	2,381,324	bb	0.00		0.00	TIC	59
32		28.507	7,575,796.5	41,397,600	bd	0.00		0.00	TIC	21.43

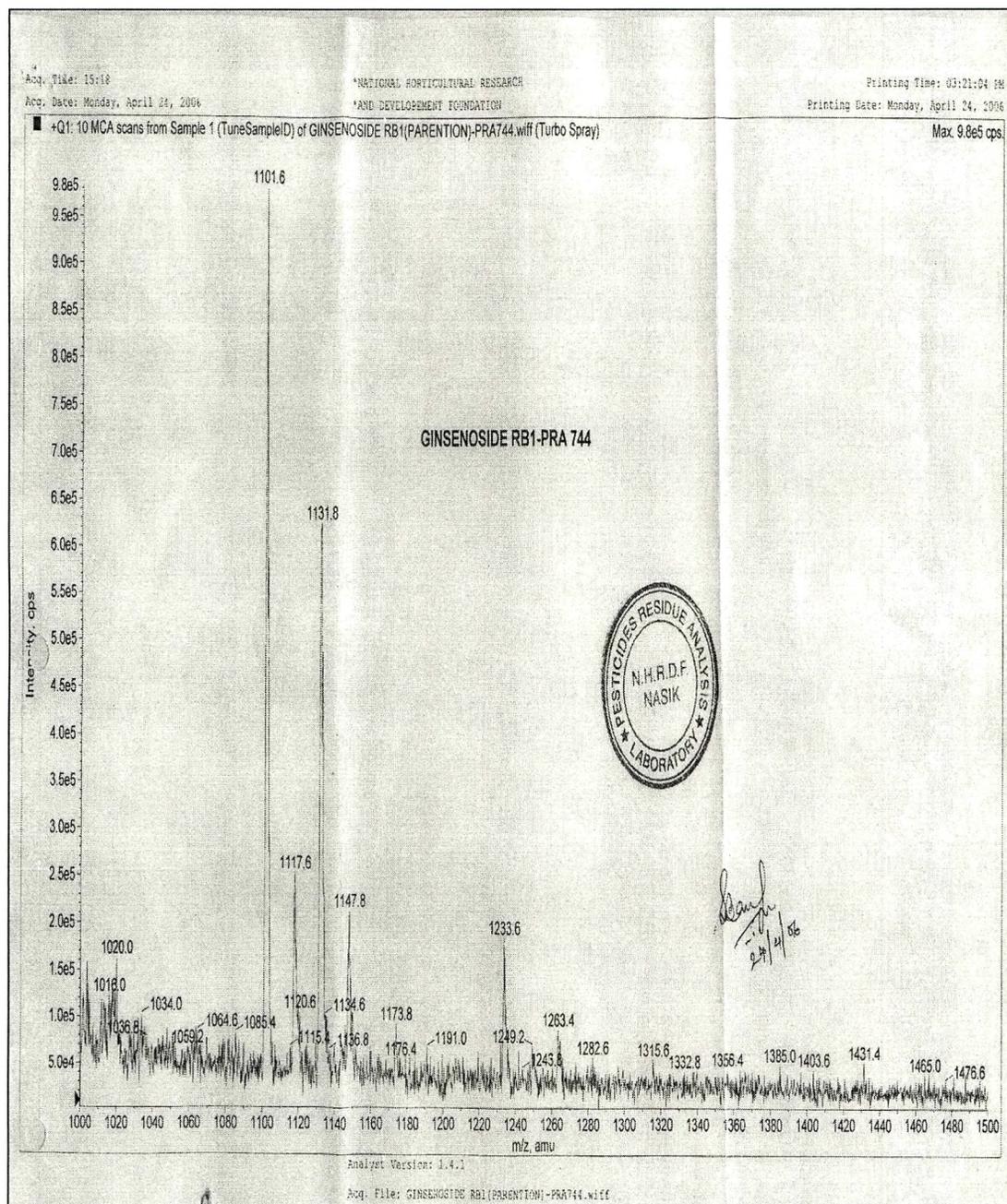


#	Name	RT	Area	Height	Bl.	Conc	Units	Area/Conc	m/z	Area %
33		28.861	476,515.8	3,093,779	db	0.00		0.00	TIC	1.35
34		29.515	51,147.0	587,054	bb	0.00		0.00	TIC	.14
35		30.082	102,999.7	818,463	bb	0.00		0.00	TIC	.29
36		30.476	68,342.3	649,920	bd	0.00		0.00	TIC	.19
37		30.663	306,997.7	2,586,529	ab	0.00		0.00	TIC	.87
38		31.331	112,366.7	600,693	bb	0.00		0.00	TIC	.32
39		31.751	77,864.3	256,943	bb	0.00		0.00	TIC	.21



Figure: 41

LC-MS chromatogram of PPE



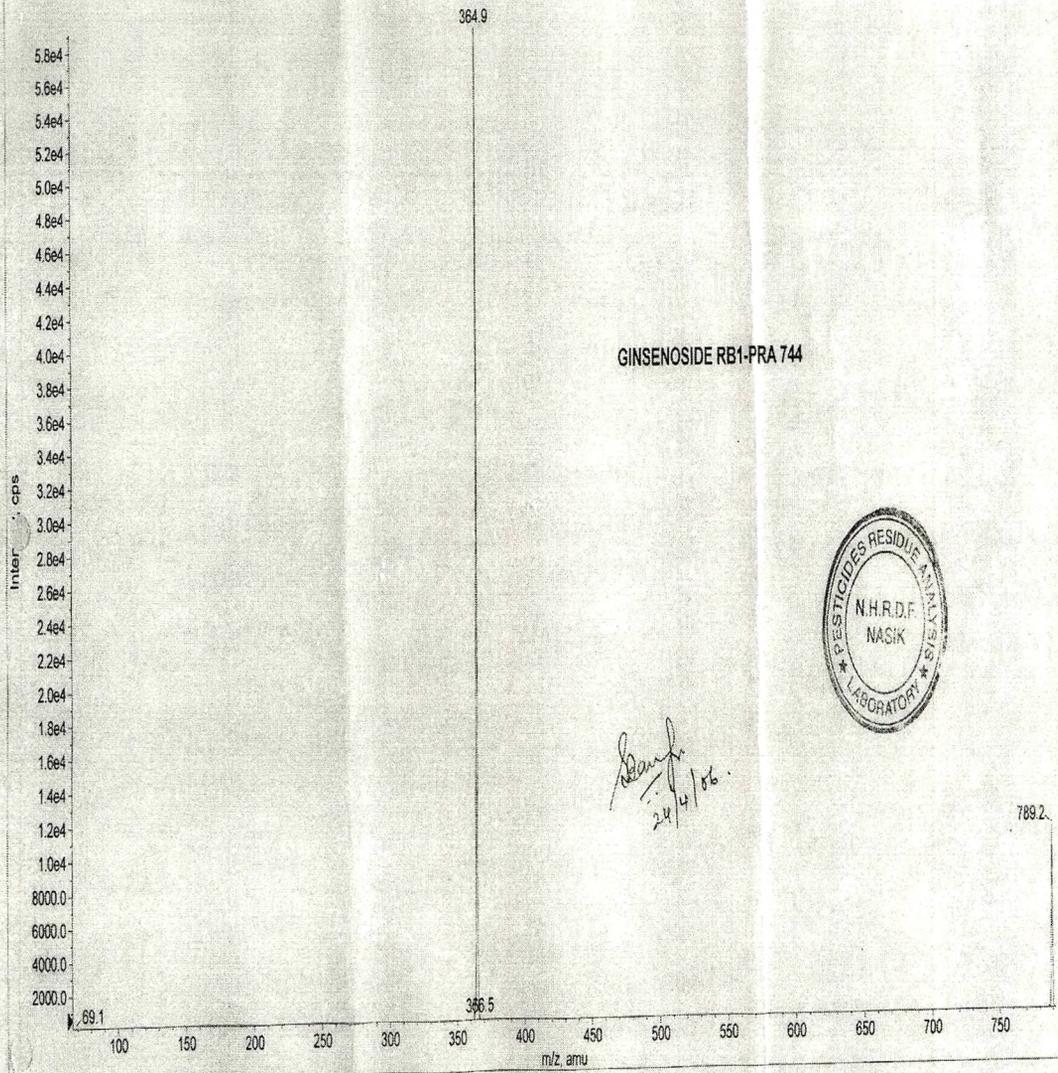
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Acq. Date: Monday, April 24, 2006

NATIONAL HORTICULTURAL RESEARCH
AND DEVELOPEMENT FOUNDATION

Printing Time: 03:54:50 PM
Printing Date: Monday, April 24, 2006

MS2 (1131.38) CE (125): 10 MCA scans from Sample 1 (TuneSampleName) of PRA744 GINSENSIDE RB 1(G1)1_FinalPrdt_Pos.wiff (Turbo ...

Max. 5.9e4 cps



Analyst Version: 1.4.1

Acq. File: PRA744 GINSENSIDE RB 1(G1)1_FinalPrdt_Pos.wiff

Acq. Time: 15:18

*NATIONAL HORTICULTURAL RESEARCH

Printing Time: 02:30:06 PM

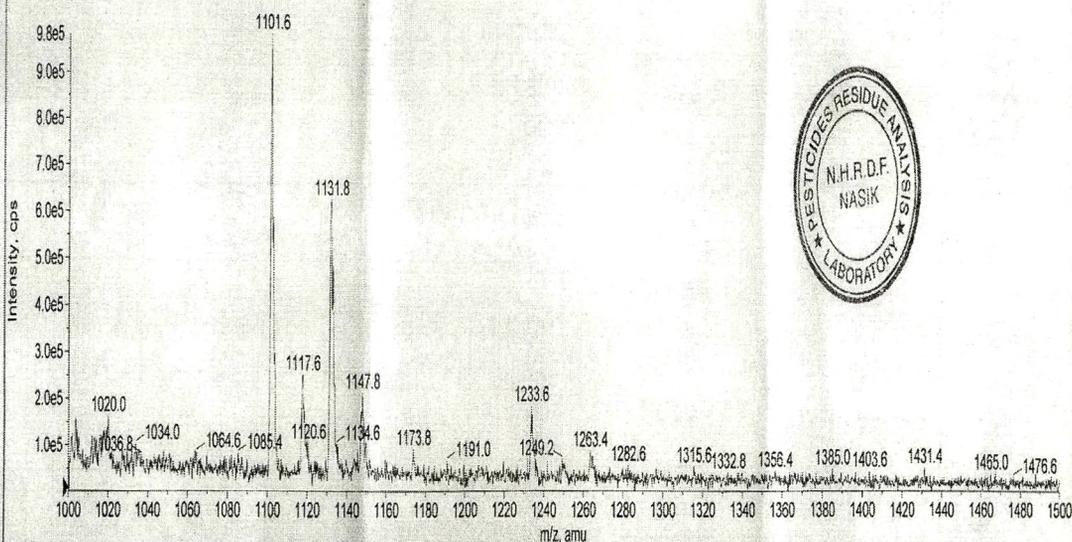
Acq. Date: Monday, April 24, 2006

*AND DEVELOPMENT FOUNDATION

Printing Date: Friday, May 05, 2006

+Q1: 10 MCA scans from Sample 1 (TuneSampleID) of GINSENSIDE RB1(PARENTION)-PRA744.wiff (Turbo Spray)

Max: 9.0e5 cps.

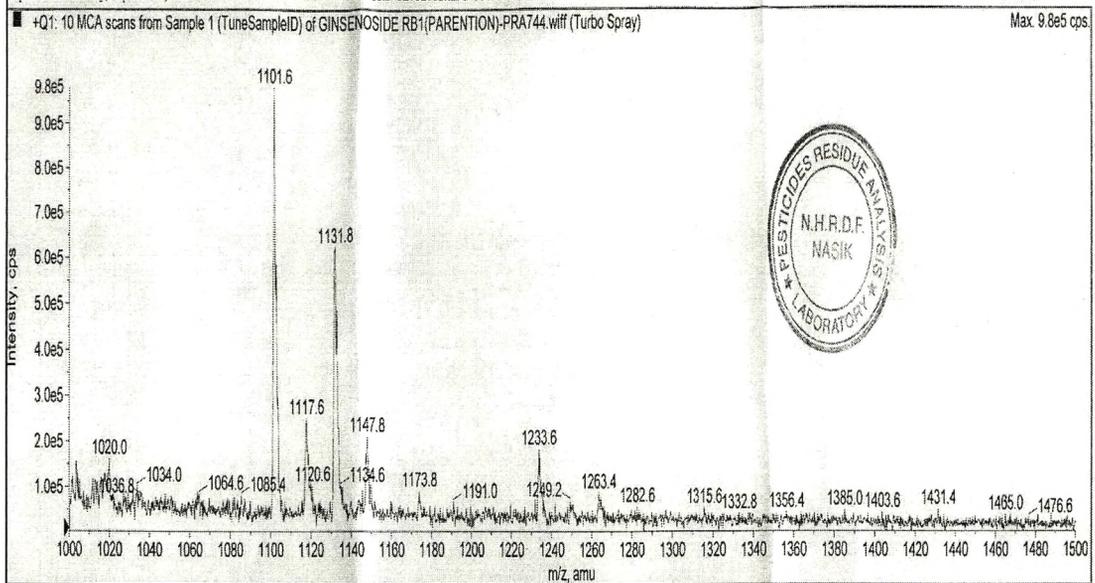


Peak List for +Q1: 10 MCA scans from Sample 1 (TuneSampleID) of GINSENSIDE RB1(PARENTION)-PRA744.wiff (Turbo Spray)"

	m/z (amu)	Intensity (cps)	Peak area (counts)	% Intensity (relative)
116	1099.0000	5.7523e4	2.6261e5	5.5980
117	1099.0000	5.7523e4	1.1505e5	5.8524
118	1099.4000	6.0024e4	1.7757e5	6.1069
119	1101.6000	9.8289e5	4.7669e6	100.0000
120	1102.6000	5.8774e5	1.7882e6	59.7964
121	1103.4000	2.9762e5	1.0254e6	30.2799
122	1104.6000	9.7539e4	1.7257e5	9.9237
123	1105.6000	7.2529e4	2.3009e5	7.3791
124	1106.4000	4.5018e4	4.5018e4	4.5802
125	1107.0000	7.0028e4	8.2533e4	7.1247
126	1107.6000	5.7523e4	7.0028e4	5.8524
127	1108.2000	5.2521e4	2.0258e5	5.3435
128	1109.0000	4.0016e4	7.0028e4	4.0712
129	1109.4000	5.5022e4	1.4756e5	5.5980

Analyst Version: 1.4.1

Acq. File: GINSENSIDE RB1(PARENTION)-PRA744.wiff



Peak List for "+Q1: 10 MCA scans from Sample 1 (TuneSampleID) of GINSENSIDE RB1(PARENTION)-PRA744.wiff (Turbo Spray)"

	m/z (amu)	Intensity (cps)	Peak area (counts)	Relative % Intensity (%)
145	1121.8000	6.2525e4	3.0262e5	6.3613
146	1123.0000	4.0016e4	4.7519e4	4.0712
147	1123.8000	6.5026e4	2.4760e5	6.6158
148	1124.0000	6.7527e4	6.7527e4	6.8702
149	1124.6000	7.0028e4	8.7535e4	7.1247
150	1125.2000	6.2525e4	1.6757e5	6.3613
151	1126.2000	5.5022e4	1.2505e5	5.5980
152	1127.0000	5.5022e4	8.0032e4	5.5980
153	1128.0000	5.0020e4	1.5756e5	5.0891
154	1129.4000	7.2529e4	2.9262e5	7.3791
155	1131.8000	6.2525e5	3.7515e6	63.6132
156	1132.6000	4.8770e5	1.6557e6	49.6183
157	1133.6000	2.3259e5	5.6523e5	23.6641
158	1134.6000	1.0254e5	3.6765e5	10.4326

Analyst Version: 1.4.1
 Acq. File: GINSENSIDE RB1(PARENTION)-PRA744.wiff