



A Toxicity Study on Vedi Annabethi Chenduram

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Abstract

The aim and objective of the study was to prepare and evaluate the safety of “Vedi Annabethi Chenduram” in animal model. Vedi Annabethi chenduram was prepared by standard operative procedure mentioned in siddha text. To evaluate it's safety acute and 28 days repeated oral toxicity studies were performed following OECD guideline 423 and 407, respectively. In acute toxicity study, the animals were treated with Vedi Annabethi Chenduram 2000mg/kg were showed tolerance with negligible toxic signs. From acute toxicity study, 1/10 and 2/10 of maximum tolerated dose ie. 200 & 400 mg/kg, were selected for further 28 days repeated oral toxicity study. The results of haematological investigations, revealed mild changes when compared with those of respective controls. The results obtained from the study showed it was safe and need further clinical studies.

Keywords: Metals, Vedi Annabethi Chenduram, Acute and sub acute toxicity.

Introduction

Siddha system of medicine is the most conservative medical system in India. In Siddha system, thousands of raw drugs are used. These drugs are categorized into three groups, namely herbal products, Metal – Mineral products and animal products. The usage of heavy metals in siddha system of medicine having some queries regarding the threatening effects of those metals which in use. Though metallic siddha medicinal formulations have high therapeutic potential when compared to allopathic drugs there is also a challenge to ensure it's safety for global acceptance. Siddha metal formulation Vedi Annabethi Chenduram is indicated for the therapeutic management of

Anaemia, Jaundice, Dropsy and Ascities. Chenduram are sulphide form of metals and minerals. There is a controversy regarding the risk of toxic metals and minerals in siddha preparations, hence toxicological parameters were investigated.

Materials and Methods

Preparation of Vedi annabethi Chenduram:

Purified Iron sulphate (1 part) is mixed with purified Potassium nitrate (1/4 part) in lemon juice and put to two or three pudamto get the chenduram. The chenduram is very effective in the treatment of anaemia, jaundice, dropsy and ascities.

Results

Acute toxicity study

Table 1. Physical and behavioral examinations

| Group no | Doses (mg/kg) | Observation sign | No of animal affected |
|-----------|-----------------|------------------|-----------------------|
| Control | Distilled water | Normal | 0 of 3 |
| Group I | 5mg/kg | Normal | 0 of 3 |
| Group II | 50mg/kg | Normal | 0 of 3 |
| Group III | 300mg/kg | Normal | 0 of 3 |
| Group IV | 2000mg/kg | Normal | 0 of 3 |

Table 2. Showed the effect of Vedi annabethi Chenduram on general behavior after 5mg, 50mg, 300mg, /kg administration

| S.No | General Behaviour | Time of Observation after | | |
|------|-------------------|--|--------------------|--------------------|
| | | Vedi annabethi Chenduram 5mg, 50mg, 300mg/kg administration. | | |
| | | 1 st hr | 3 rd hr | 4 th hr |
| 1 | Sedation | - | - | - |
| 2 | Hypnosis | - | - | - |
| 3 | Convulsion | - | - | - |
| 4 | Ptosis | - | - | - |
| 5 | Analgesia | - | - | - |
| 6 | Stupor Reaction | - | - | - |
| 7 | Motor activity | - | - | - |
| 8 | Muscle Relaxant | - | - | - |
| 9 | CNS Stimulant | - | - | - |
| 10 | CNS Depressant | - | - | - |
| 11 | PiloErection | - | - | - |
| 12 | Skin Colour | - | - | - |
| 13 | Lacrimation | - | - | - |
| 14 | Stool Consistency | - | - | - |

‘+’ PRESENT & ‘-’ ABSENT

Table 3. Showed the effect of Vedi annabethi Chenduram (2000mg/kg) on general behavior after single oral administration in mice

| S.No | General Behaviour | Time of Observation after | | | | | |
|------|-------------------|----------------------------|---|--------------------|---|--------------------|--|
| | | Vedi annabethi Chenduram | | | | | |
| | | (2000mg/kg) administration | | | | | |
| | | 1 st hr | | 3 rd hr | | 4 th hr | |
| 1 | Sedation | - | - | - | - | - | |
| 2 | Hypnosis | - | - | - | - | - | |
| 3 | Convulsion | - | - | - | - | - | |
| 4 | Ptosis | - | - | - | - | - | |
| 5 | Analgesia | - | - | - | - | + | |
| 6 | Stupar Reaction | - | - | - | - | - | |
| 7 | Motor activity | - | - | - | - | + | |
| 8 | Muscle Relaxant | - | - | - | - | - | |
| 9 | CNS Stimulant | - | - | - | - | - | |
| 10 | CNS Depressant | - | - | - | - | - | |
| 11 | Pilo Erection | - | - | - | - | - | |
| 12 | Skin Colour | - | - | - | - | - | |
| 13 | Lacrimation | - | - | - | - | - | |
| 14 | Stool Consistency | - | - | - | - | - | |

‘+’PRESENT&‘-’ABSENT

Sub-Acute toxicity study

Table 4. Effect of Vedi annabethi Chenduram on body weight during 28 days treatment in rats

| Groups | Drug Treatment | Body Weight (gms) | | | | |
|--------|---|---------------------|---------------------|----------------------|----------------------|----------------------|
| | | 1 st Day | 7 th Day | 14 th Day | 21 st Day | 28 th Day |
| I | Control | 155.36± | 158.58± | 162.65± | 169.71± | 180.54± |
| | DistilledWater (1ml/kg, p.o) | 2.87 | 2.46 | 1.98 | 1.90 | 2.35 |
| II | Vediannabethi Chenduram (200mg/kg, p.o) | 166.67± | 168.34± | 174.53± | 177.76± | 180.04± |
| | | 2.22 | 3.42 | 4.23 | 3.22 | 2.76 |
| III | Vediannabethi Chenduram (400mg/kg, p.o) | 160.07± | 162.88± | 167.32± | 169.43± | 175.43± |
| | | 2.82 | 2.65 | 2.37 | 3.22 | 4.00 |

Values are in mean± SEM(n=6)

*P<0.05,**P<0.01,***P<0.001 VsControl

Figure 1. Effect of Vedi annabethi Chenduram on bodyweight during 28 days treatment in rats

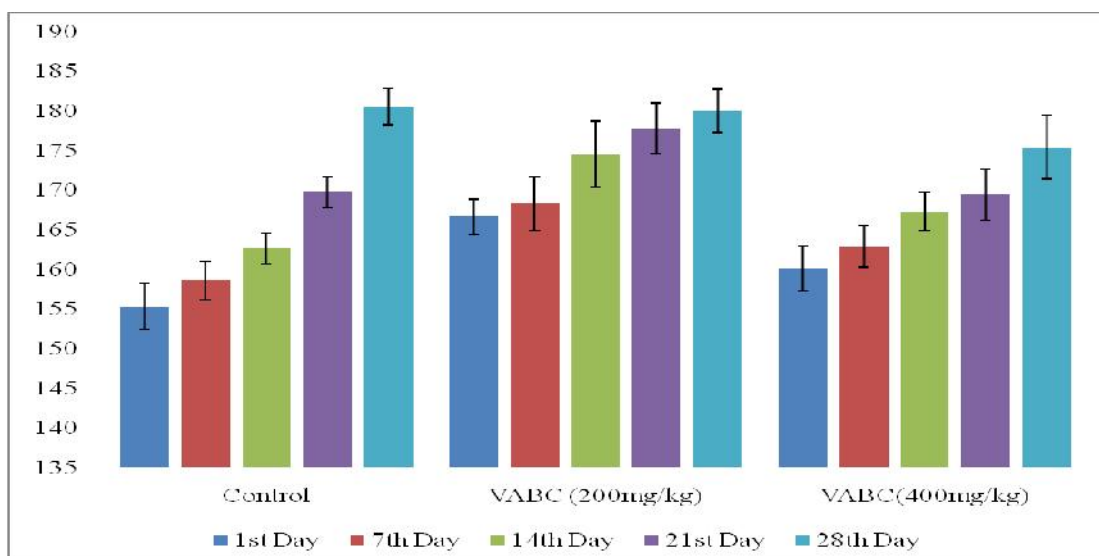


Table 5.Effect of Vedi annabethi Chenduramon food intake during 28 days Treatment in rats

| Groups | Drug Treatment | Food Intake(gms) | | | | |
|--------|--|---------------------|---------------------|----------------------|----------------------|----------------------|
| | | 1 st Day | 7 th Day | 14 th Day | 21 st Day | 28 th Day |
| I | Control | 24.36± | 23.66± | 23.23± | 24.32± | 25.59± |
| | Distilled Water (1ml/kg. p.o) | 1.23 | 2.07 | 2.23 | 2.31 | 2.06 |
| II | Vediannabethi Chenduram (200mg/kg.p.o) | 25.54± | 26.71± | 27.90± | 27.31± | 28.24± |
| | | 1.74 | 1.87 | 2.54 | 2.03 | 1.54 |
| III | Vediannabethi Chenduram (400mg/kg.p.o) | 24.65± | 25.07± | 26.34± | 27.86± | 27.48± |
| | | 2.75 | 1.72 | 2.15 | 2.57 | 2.37 |

Values are in mean±SEM (n=6)

*P<0.05,**P<0.01,***P<0.001VsControl

Figure 2. Effect of Vedi annabethi Chenduramon food intake during 28 days treatment in rats

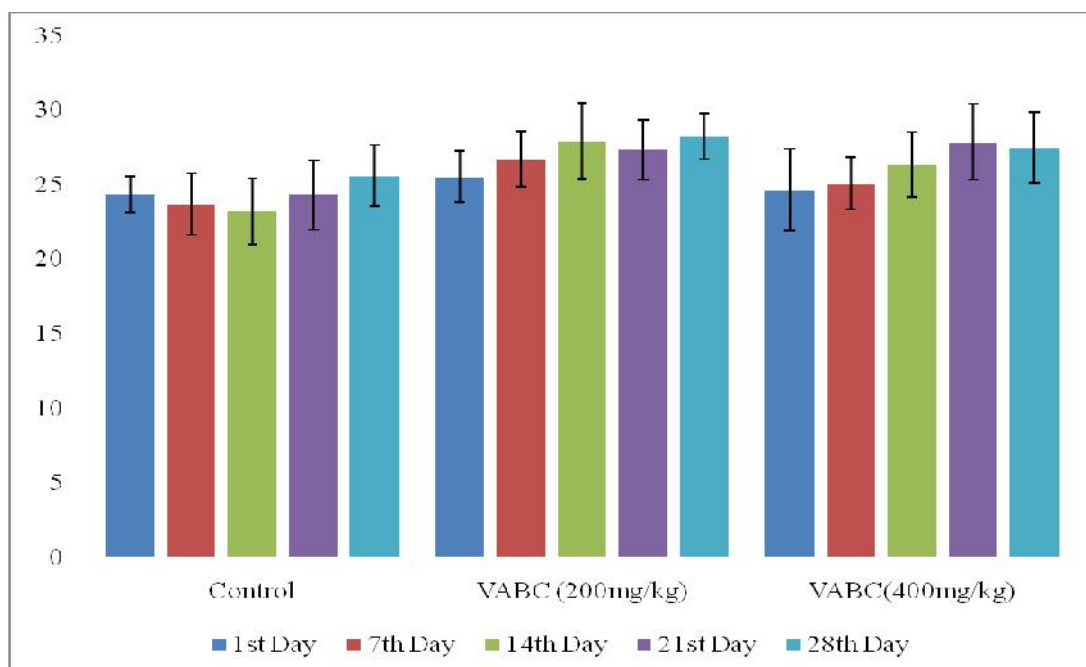


Table 6. Effect of VEDI annabethi Chenduram on water intake during 28 days treatment in rats

| Groups | Drug Treatment | Water Intake (ml) | | | | |
|--------|----------------------------------|---------------------|---------------------|----------------------|----------------------|----------------------|
| | | 1 st Day | 7 th Day | 14 th Day | 21 st Day | 28 th Day |
| I | Control | 66.37± | 69.41± | 72.55± | 70.23± | 75.58± |
| | Distilled Water (1ml/kg, p.o) | 2.45 | 3.09 | 4.33 | 3.39 | 4.98 |
| II | Vediannabethi Chenduram | 67.09± | 70.02± | 69.55± | 70.24± | 72.45± |
| | (200mg/kg,p.o) | 2.32 | 3.11 | 4.54 | 4.22 | 2.89 |
| III | Vediannabethi Chenduram | 66.43± | 66.55± | 69.54± | 71.43± | 72.22± |
| | (400mg/kg,p.o) | 4.10 | 5.08 | 4.65 | 4.45 | 5.21 |

Values are in mean±SEM(n=6)

*P<0.05,**P<0.01,***P<0.001 VsControl

Figure 3. Effect of VEDI annabethi Chenduram on water intake during 28 days treatment in rats

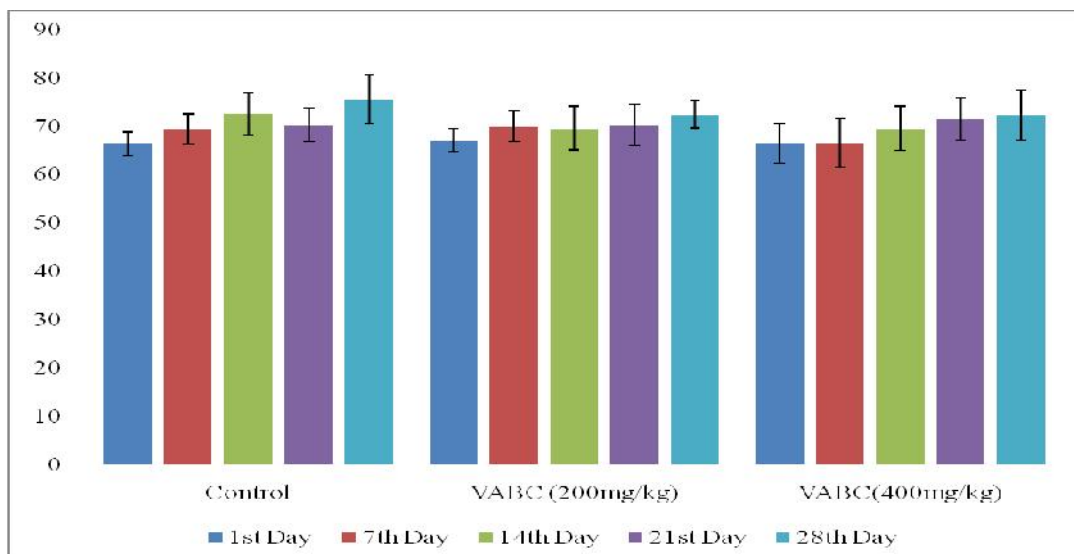


Table 7. Shows the effect of VEDI annabethi Chenduram on RBC, WBC and Hb In rats after 28 days treatment

| Groups | Drug Treatment | RBC million cells/cmm | WBC cells/cmm | Haemoglobin gm% |
|--------|--|-----------------------|-------------------|-----------------|
| I | Control Distilled Water (1ml/kg, p.o) | 4.21± 0.40 | 8696.81± 67.32 | 14.40± 0.59 |
| II | Vediannabethi Chenduram (200mg/kg.p.o) | 4.51± 0.17 | 8092.54± 69.98 | 14.68± 0.96 |
| III | Vediannabethi Chenduram (400mg/kg.p.o) | 4.34± 0.22 | 8587.05± 79.61 | 14.93± 0.43 |

Values are in mean ± SEM(n=6)

*P<0.05,**P<0.01,***P<0.001VsControl

Figure 4. Shows the effect of VEDI annabethi Chenduramon RBC and Hb in rats After 28 days treatment.

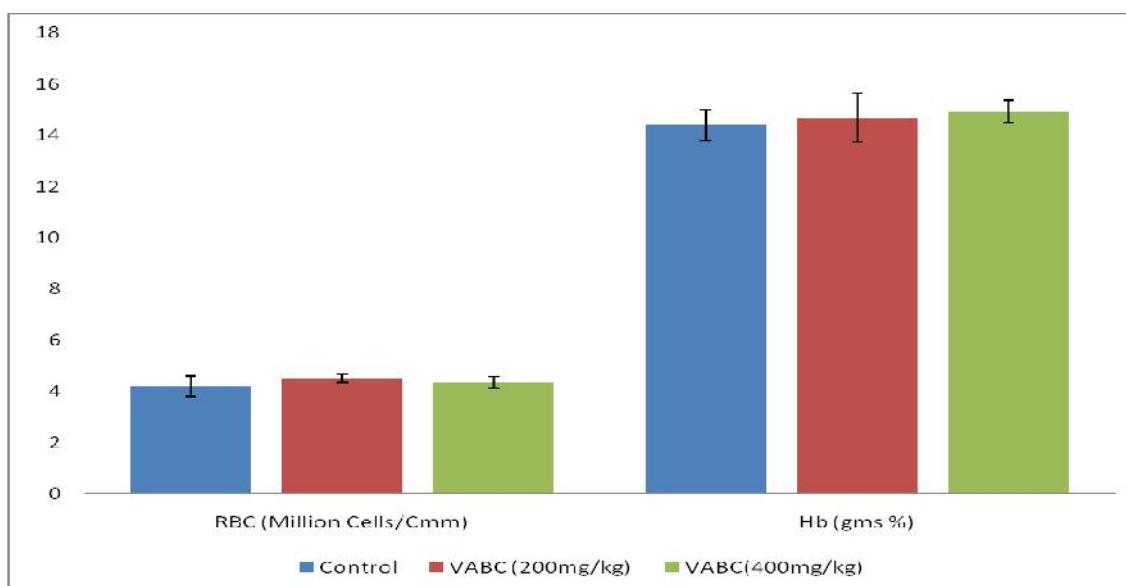


Figure 5. Shows the effect of VEDI annabethi Chenduram on WBC in rats after 28 days treatment

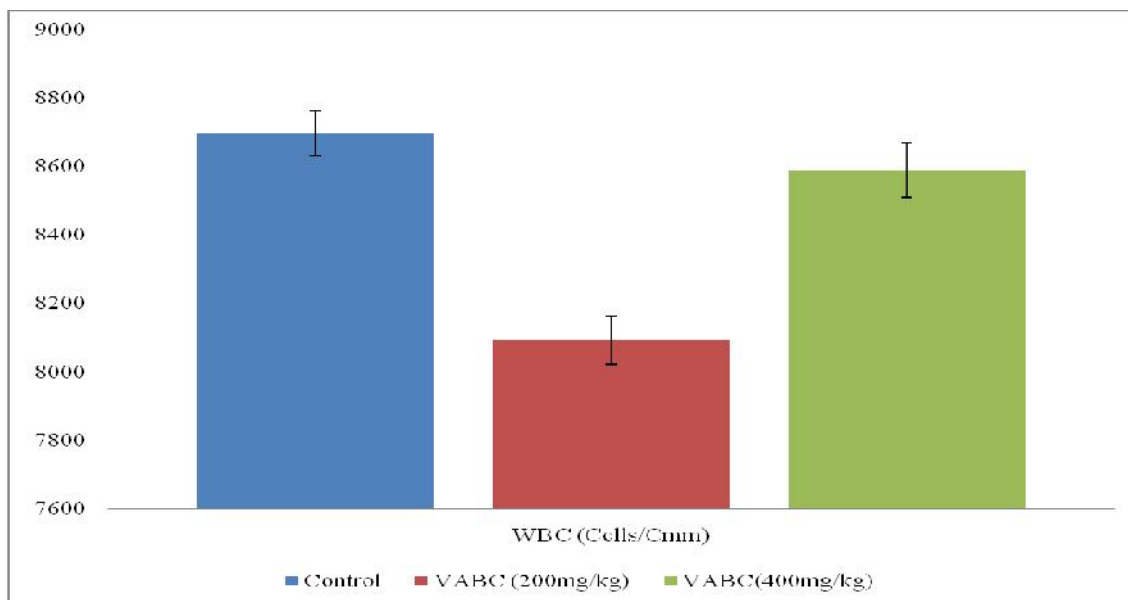


Table 8. Shows the effect of VEDI annabethi Chenduram on Differential Count In rats after 28 days treatment

| Groups | Drug Treatment | Differential Count% | | | |
|--------|--|---------------------|--------------------|-----------------|-------------------|
| | | <i>Neutrophils</i> | <i>Eosinophils</i> | <i>Monocyte</i> | <i>Lymphocyte</i> |
| I | Control Distilled Water (1ml/kg, p.o) | 31.72± 1.60 | 1.93±0.15 | 3.89± 0.19 | 63.17± 3.76 |
| II | Vediannabethi Chenduram (200mg/kg,p.o) | 33.39± 1.97 | 2.04±0.14 | 3.10± 0.15 | 60.56± 1.64 |
| III | Vediannabethi Chenduram (400mg/kg,p.o) | 32.00± 2.09 | 1.98±0.09 | 3.66± 0.08 | 61.34± 2.22 |

Values are in Mean±SEM(n=6)

*P<0.05,**P<0.01,***P<0.001 Vs Control

Figure 6. Shows the effect of Vedi annabethi Chenduram on Differential Counts In rats after 28 days treatment

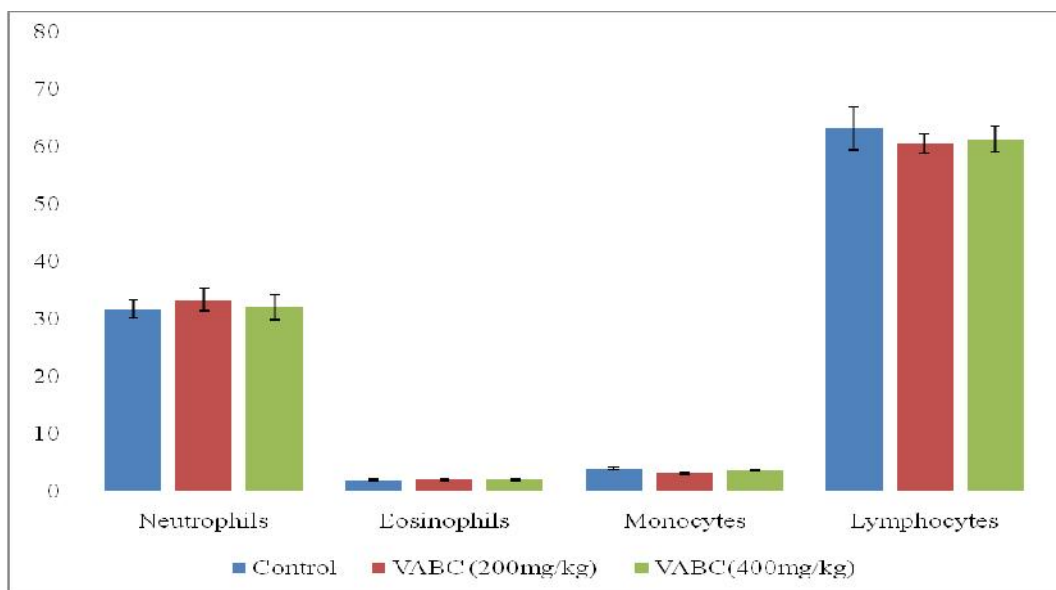


Table 9. Shows the effect of Vedi annabethi Chenduram on Hepatic Functions (SGPT, SGOT and ALP) in rats after 28 days treatment.

| Groups | Drug Treatment | SGPT (IU/L) | SGOT (IU/L) | ALP (IU/L) |
|--------|--|-------------|-------------|--------------|
| I | Control Distilled Water (1ml/kg, p.o) | 82.14±3.06 | 148.28±4.71 | 287.52±11.76 |
| II | Vediannabethi Chenduram(200mg/kg, p.o) | 86.18±3.08 | 153.87±4.19 | 275.51±12.46 |
| III | Vediannabethi Chenduram(400mg/kg, p.o) | 85.30±4.67 | 152.60±5.03 | 281.94±9.06 |

Values are in mean±SEM(n=6)

*P<0.05,**P<0.01,***P<0.001VsControl

Figure 7.Shows the effect of VEDI Annabethi Chenduram on Hepatic Functions In rats after 28 days treatment

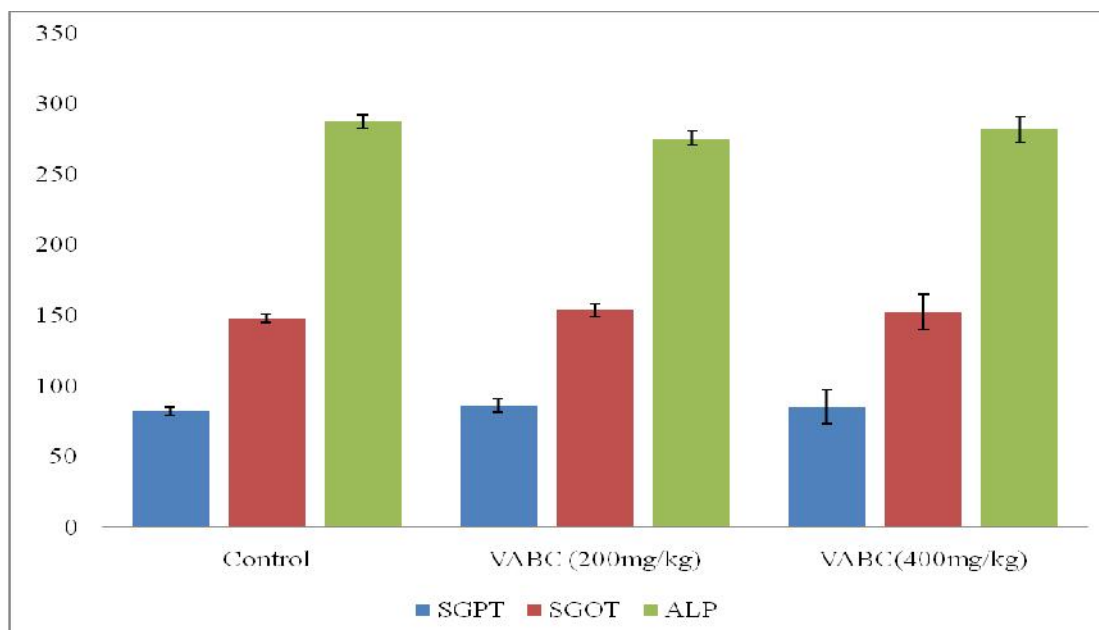


Table 10.Shows the effect of VEDI Annabethi Chenduram on Kidney Functions in Rats after 28 days treatment

| Groups | Drug Treatment | Urea (mg/dl) | Creatinine (mg/dl) |
|------------|---|--------------|--------------------|
| I | Control Distilled Water (1ml/kg, p.o) | 39.79±3.00 | 0.94±0.03 |
| II | Vediannabethi Chenduram (200mg/kg, p.o) | 40.97±2.82 | 1.02±0.04 |
| III | Vediannabethi Chenduram (400mg/kg, p.o) | 42.00±2.78 | 0.96±0.02 |

Values are in mean±SEM(n=6)

*P<0.05,**P<0.01,***P<0.001VsControl

Figure 8.Shows the effect of Vedi annabethi Chenduram on Kidney Functions (Creatinine) in rats after 28 days treatment

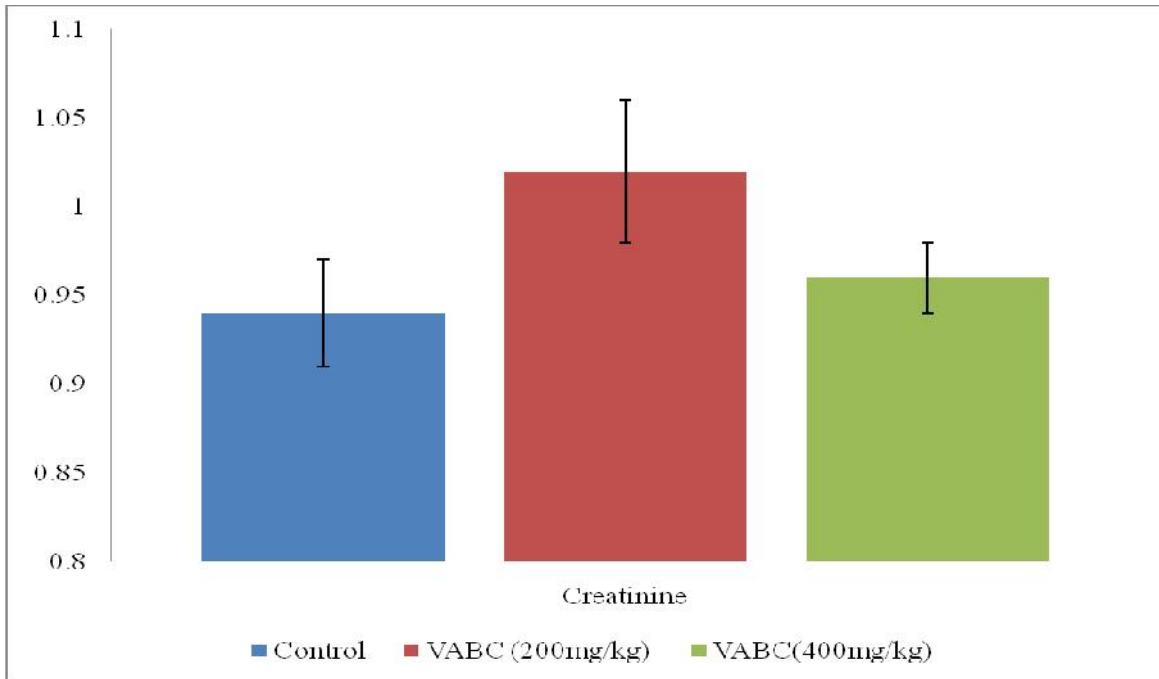
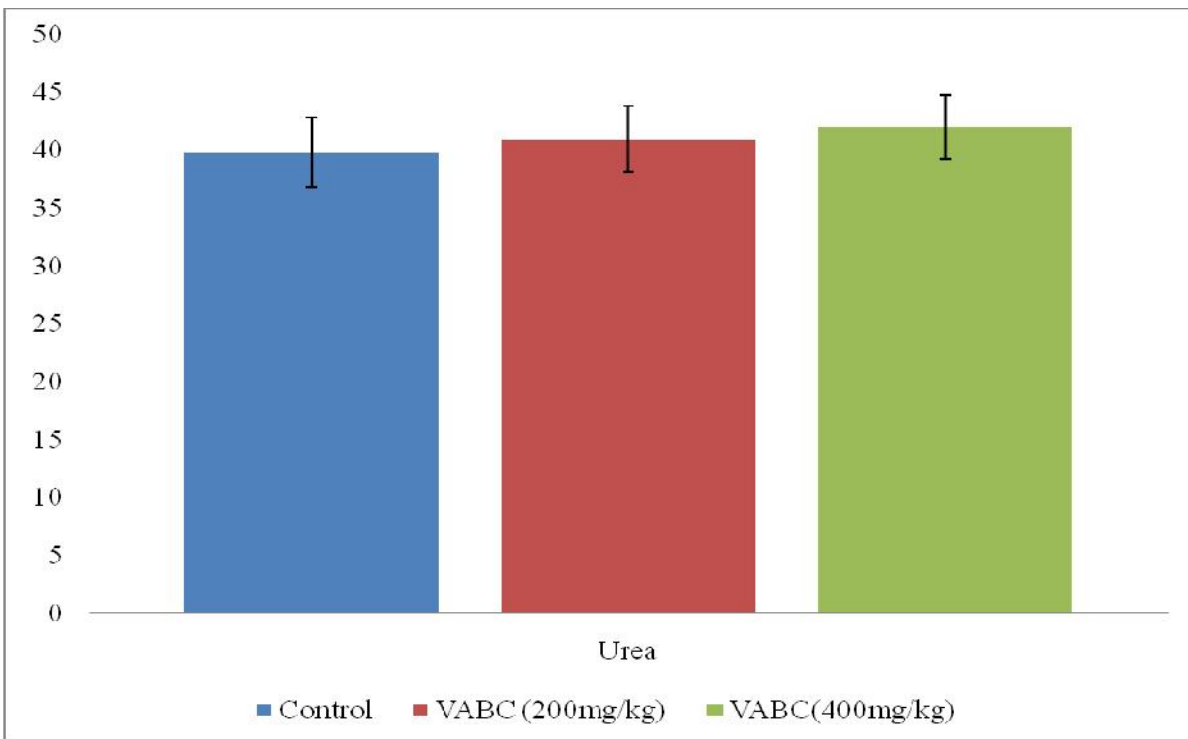


Figure 9.Shows the effect of Vedi annabethi Chenduram on Kidney Functions (Urea) in rats after 28 days treatment



Discussion

The results of acute toxicity study of *Vedi annabethi Chenduram* were shown on table 1-3. There was no mortality with the *Vedi annabethi Chenduram* after 72 hrs even at higher dose of 2000mg/kg. There was no significant change in general behavior after 1st and 24 hrs. After 72hrs of *Vedi annabethi Chenduram* administration (2000mg/kg), the animals showed analgesic and increase in motor activity. From the results of acute toxicity study, *Vediannabethi Chenduram* was found to be safe in mice.

From acute toxicity study, 1/10 and 2/10 of maximum tolerated dose ie, 200&400mg/kg, were selected for further sub-acute toxicity study.

In sub-acute toxicity study, body weight, food intake and water intake were observed on 1st, 7th, 14th, 21st and 28th day of *Vedi annabethi Chenduram* administration.

The effect of *Vedi annabethi Chenduram* on body weight during 28 days treatment in rats was given in table 4 and figure 1. There was no significant change in the body weight compared to control with both the doses of *Vediannabethi Chenduram* during 28 day treatment.

The effect of *Vedi annabethi Chenduram* on food intake during 28 days treatment in rats was given in table 5 and figure 2. *Vedi annabethi Chenduram* did not alter the food intake at both the dose levels as compared to control during the 28 days treatment. It indicates that it does not influence food intake.

The effect of *Vedi annabethi Chenduram* on water intake during 28 days treatment in rats was given in table 6 and figure 3. *Vedi annabethi Chenduram* did not alter the water intake at both the dose levels as compared to control during the 28 days treatment. There was no significant change in water intake as compared to control.

Table 7, figure 4 and 5, shows the effect of *Vedi annabethi Chenduram* on haematological parameters like RBC, WBC and Hb in rats after 28 days treatment.

Both the doses of *Vedi annabethi Chenduram* did not produce any significant change in RBC, WBC and Hb compared to control.

The effect of *Vedi annabethi Chenduram* on Differential Count in rats after 28 days treatment was shown on table and figure 6. Both the doses of *Vediannabethi Chenduram* did not show any significant change in differential counts like Neutrophils, Eosinophils, Monocyte and Lymphocytes. From the effect of *Vediannabethi Chenduram* on hematological parameters it was found that it does not produce any toxicity in haemopoietic system.

The effect of *Vedi annabethi Chenduram* on hepatic functions in rats after 28 days treatment was shown on table 9 and figure 7. The hepatic enzymes (SGPT, SGOT and ALP) were remain normal with both the doses of *Vedi annabethi Chenduram* and the values were similar as that of control group which received distilled water. From the result of hepatic enzymes it was found the *Vedi annabethi Chenduram* did not produce any toxic effects on liver in rats.

The effect of *Vedi annabethi Chenduram* on renal functions in rats after 28 days treatment was shown on table 10 and figure 8 & 9. Both the doses of *Vedi annabethi Chenduram* does not showed any significant change in urea and creatinine after 28 days treatment compared to control which indicates, *Vediannabethi Chenduram* was free from renal toxicity.

Conclusion

Vedi annabethi Chenduram was studied for its acute and sub-acute toxicity effects using laboratory animals. In acute toxicity study, *Vedi annabethi Chenduram* did not produce any specific toxicity and mortality even at the dose of 2000mg/kg in mice.

In sub-acute toxicity study, 200 and 400mg/kg of *Vedi annabethi Chenduram* was used and it was administered once daily for 28 days through oral route. *Vedi annabethi Chenduram* did not alter the body weight, food intake and water intake during the study period.

After 28 days the blood was subjected to liver and kidney function test. Both the doses of *Vediannabethi Chenduram*, did not show any significant changes in the functional parameters of liver and kidney.

From the study it is concluded that, *Vedi annabethi chenduram* is found to be safe in long term administration clinical practice upto the dose of 400mg/kg.

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