

Case Study

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## *Anamirta cocculus* Toxicity in Malnad Gidda Cattle: A Case Report

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### ABSTRACT

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In Tirthahalli of Shivamogga District of Karnataka State, 11 Malnada Gidda cattle of different age group succumbed to toxicity and exhibited the clinical signs of anorexia, shivering, nervousness, lethargy and wobbling gait. Ailing animals were treated symptomatically with diazepam, xylazine, fluids and B-complex vitamins with administration of activated charcoal. On obtaining the history and visit to the affected area, it was evident that the animals had consumed the fruits of the plant *Anamirta cocculus*. Blood analysis of the ailing animals revealed no change in the haematological and biochemical parameters except hyperglycaemia. Post mortem finding revealed extensive hemorrhage in the brain with no change in the other organs.

### Introduction

Plant toxicity is a common cause of the morbidity and mortality of cattle in Western Ghats of Karnataka State. Malnad Gidda cattle are habitat of Western Districts of Karnataka State and let out for grazing in forest and do have more access to toxicity of plants. It is said that these cattle do can differentiate the poisonous from edible plant which seems to be false. Because of the edible

nature of the plants like *Embelia tserium* *Cotton* and *Mimosa invisa* cattle and buffaloes do consume them and succumb to toxicity.

They also succumb to toxicity by accidental consumption of leaves *Ficus tsjahela* and *Hevea brasiliensis* cut by farmers (Lohith *et al.*, 2014; Shridhar *et al.*, 2014; Shridhar, 2017). *Anamirta cocculus* is a climbing plant from India and other parts of Southeast Asia.

It is known for its large stems of white wood and scented flowers (Figure 1 and 2). It produces small fruits with sweet pulp (Verpoorte *et al.*, 1981). During the fruiting season, Malnad Gidda cattle do consume the fruits fallen on the ground because of the sweet nature of the pulp of the fruits and also rarely consume the leaf of the plant when there is scarcity of fodder. The seed of fruits of the plant do contain a potent toxin picrotoxin, which is a very strong neurotoxin in all vertebrates affecting CNS. Fresh or dry semi-ripe fruits with or without the fruit pulp is ground and used as fish stupefying agent. In India and South-East Asia the fruit of *Anamirta cocculus* is used mainly as a fish poison (Duman *et al.*, 2001; Jijith *et al.*, 2016).

The data on toxicity features of *Anamirta cocculus* in cattle is scanty. Hence, the present study was aimed to evaluate the toxic feature of the plant and to study the changes in hematological and serum biochemical changes and also to evaluate the effectiveness of treatment.

### **Case study**

In Chikkahodala village, Tirthahalli Taluk, Shivamogga District of Karnataka, 12 Malnad Gidda ( 8 Female and 4 males) cattle with age ranging from 5-11 years reported to be exhibiting the clinical signs of anorexia, shivering, nervousness, lethargy and wobbling gait. Out of 12 animals, 7 died ( 5 female and 2 males) succumbed to death after exhibiting the said clinical signs within a span of 24 h. The onset of the toxicity was initiated with abnormal gait causing in coordination during getting up and walking. Excitement and salivation were the early clinical signs later with severe excitation. There was clonic convulsions with paddling of the limbs. There was blurred vision in affected animals confirmed by diminished palpebral reflex

(Figure 3 and 4). There was projectile regurgitation. There was anxiety in mild to moderate convulsions were observed in few animals. The site was visited and it was observed that all the cattle had consumed the fruits of the plant *Anamirta cocculus* which was present in the grazing area and it was the fruiting season.

The temperature, respiratory rate and heart rate were recorded timely. Blood samples from the affected Malnad Gidda cattle were obtained at the intervals of 24, 48, 72 and 96 h following the onset of the signs of toxicity. To serve as the control, the blood was also drawn from the other healthy Malnad Gidda cattle without toxicity.

The Malnad Gidda cattle exhibiting the clinical signs of the toxicity were treated with diazepam @ 0.5 mg/kg slow IV, xylazine 0.1-0.2 mg/kg IM, B-complex vitamins, IM, intravenous administration of 5-10 ml/kg of 10 % dextrose solution, activated charcoal @ 2g/kg orally twice at 10 to 12 h interval for three consecutive days.

Alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), serum creatinine (CRT), calcium, magnesium, phosphorus and glucose were estimated in serum of the affected as well as the normal control Malnad Gidda animals.

Postmortem of animals succumbed to death was conducted and the gross lesions were noted. Representative brain, heart, spleen, intestine, kidney, liver, rumen, and abomasum tissue samples were collected for histopathology at 10 % neutral buffered formalin (NBF).

### **Results and Discussion**

Examination of the affected animals revealed increased body temperature (105.7°F),

tachycardia (115/min) and tachypnoea (30/min). This might be due to the convulsive episodes and excitation followed by depression similar to that is observed in many neurotoxicities and plant toxicities like *Ficus tsjahela* (Shridhar, 2017).

The important clinical sign of *Anamirta cocculus* toxicity in Malnad Gidda cattle included clinical signs of, shivering, anorexia, nervousness, lethargy and wobbling gait. Most of the animals (7/11) succumbed to death indicated the severity of the toxicity. Few of the clinical signs of the toxicity resembled to neurotoxicity in *Ficus tsjahela* toxicity as reported earlier (Shridhar *et al.*, 2014; Shridhar, 2017).

Picrotoxin is the active principle of the fruit pulp of the plant *Anamirta cocculus*. Picrotoxin is a convulsant and in larger doses induces clonic convulsions and cardiac dysrhythmias. Picrotoxin induces the convulsions by blocking  $\alpha 2$  homomeric glycine receptors (Newland and Cull-Candy, 1992, Wang *et al.*, 2007). Death occurs rapidly due to respiration failure, or slowly from gastrointestinal symptoms, particularly the medulla oblongata and respiratory centre.

The acute death in the present study in affected cattle might be due to respiratory failure and rather than gastrointestinal signs as they were less evident. The clinical signs exhibited by the Malnad Gidda cattle do resemble the toxicity features of many neurotoxic plants especially *Ficus tsjahela* toxicity in cattle and buffaloes (Shridhar *et al.*, 2014; Shridhar, 2017).

The surviving Malnad Gidda cattle exhibiting the clinical signs of toxicity were administered with 0.5 mg/kg diazepam slow IV, 5-10 ml/kg dextrose solution IV along with B-complex vitamins for 3 days in an interval of 24 h. Improvement in the condition

was observed by getting up and consumption of feed or water followed by voiding the dung or urine. On day 4 of the treatment most of the animals got recovered. There was no re occurrence of the toxicity signs in any of the treated Malnad Gidda animals. This might indicate that the toxin might have excreted from the body (Shridhar, 2017).

Administration of diazepam @ 0.25-0.5 mg/kg slow IV in an interval of 10-12 h and xylazine @ 0.1-0.2 mg/kg IM made satisfactory recovery of the treated animals subsiding the clinical signs and restoring their normal physical and physiological activity within 72 h.

Diazepam is a benzodiazepine that exerts anticonvulsant, sedative, anxiolytic, musclerelaxant, and amnesic effects. These effects are brought by mimicking gamma aminobutyric acid (GABA) receptor which are inhibitory in nature in CNS. It is also a drug for short term treatment of epilepsy. Being a good sedative, it has got the anti-anxiety property.

The recovery of the animals might be attributed to this. Hence, the clinical signs might have subsided (Mandrioli *et al.*, 2008; Riss *et al.*, 2008). Picrotoxin initiates its action through GABA receptor. The satisfactory clinical recovery of the Malnad Gidda animals in *Anamirta cocculus* toxicity indicated the dose and interval selected might be appropriate (Booth and McDonald, 1998). Pankaj Kumar Patel *et al.*, (2018) also managed the calf with ivermectin toxicity exhibiting the neurological signs with administration of diazepam.

One of the the preferred sedative in cattle is xylazine which is administered IM @ 0.1-0.2 mg/kg for long time of action. Xylazine is a anticonvulsant sedative and one of the most commonly used  $\alpha 2$  adrenergic receptor

agonist in cattle. In the present study, it was used @ 0.1-0.2 mg /kg IM. In this dose, it reversed the toxicity clinical signs (Zuhair *et al.*, 2010; Lakech and Kindalem, 2019; Michael *et al.*, 2015).

In the present study, activated charcoal was administered at the dose of 2 g/kg orally as a 1:8 slurry which might have adsorbed the toxins from the gut. The activated charcoal is a black powder available as a laboratory grade chemical which produces a fine suspension when mixed with water. In much toxicity in cattle, activated charcoal is used for the treatment effectively.

Activated charcoal is administered in toxicities in early stage before absorption of the toxin/s into circulation or during the onset of clinical signs of the toxicity to inhibit the further absorption of the toxicants in the gut.

Many plant toxicities were treated effectively by administration of activated charcoal in similar dose with examples of Lantana toxicity (Michael and Coralie Stewart, 1984, Gupta *et al.*, 2019) and Yellow tulp (*Moraea pallid*) toxicity (Snyman *et al.*, 2009).

Vital dietary supplements include B-complex vitamins in which thiamine are an important vitamin which is needed for metabolism of carbohydrates. Other important components of B-complex vitamins include riboflavin and cobalamin. In carbohydrate metabolism thiamine is a cofactor and produces energy in carbohydrate metabolism for formation of thiamine pyrophosphate.

Opisthotonus, circling movements, listlessness, muscle tremors in ruminants will be exhibited by ruminants in impairment in its synthesis or deficiency affects that the carbohydrate metabolism. Due to deficiency of thiamine, polioencephalomalacia (PEM) a non-infectious nutritional deficiency disease

in which there will be the neurological signs. The clinical signs in present study do have similarity to PEM. In the present study, B-complex vitamins containing thiamine hydrochloride with administration of dextrose might augmented the recovery of the toxicity affected Malnad Gidda animals (Christiane, 2017, Tolga *et al.*, 2010).

In estimated biochemical parameters, an increase ( $P < 0.05$ ) in blood glucose of the affected animals during the course of toxicity which returned to normal at 96 h with no change in ALT, AST, BUN, CRT, calcium, magnesium and phosphorus was noticed (Table 1). There was no change in the hematological parameters in the present study (Table 2).

In the present study there was an increase in the blood glucose concentration which returned to normal after the animal's recovery. This might be attributed to clonic convulsions leading to increased skeletal muscles activity might be the cause of hyperglycemia.

Increased skeletal muscle activity requires more glucose. Acute hyperglycemia during clonic convulsions suggested reflux increase in muscle activity and increase in blood glucose concentration (Ratnasooriya *et al.*, 1992, Geetha *et al.*, 1994)

There was no change in the hematological parameters during the course of toxicity indicating that the toxicity had not affected system and this is accordance with the finding of few workers who also noted that no change in such parameters (Mathew *et al.*, 2014).

Extensive hemorrhages in the brain of the affected Malnad Gidda animals was observed during the post mortem. There were degenerative changes in the neurons and glial cells (Figure 5 and 6).

**Table.1** Biochemical profile of Malnad Gidda cattle affected with *Anamirta cocculus* toxicity (Mean±SEM)

Parameter	Apparently healthy Malnad Gidda cattle (n=6)	Malnad Gidda cattle affected with <i>Anamirta cocculus</i> toxicity (n=5)				
		0 hour	24 hours <sup>#</sup>	48 hours <sup>#</sup>	72 hours	96 hours
Alanine amino Transferase (ALT in U/L)	31.5±3.19	28.17±1.99	29.68±2.58	26.30±2.83	26.53±2.74	28.82±2.66
Aspartate amino Transferase (AST in U/L)	59.25±2.58	56.87±2.62	59.97±2.26	59.39±2.68	56.83±2.63	57.36±1.65
Blood Urea Nitrogen (BUN in U/L)	19.66±1.62	21.38±2.64	23.16±1.25	20.73±1.45	19.25±2.88	21.25±1.98
Creatinine (mg/dl)	1.13±0.23	1.29±0.37	1.72±0.23	1.98±0.95	1.89±0.63	1.63±0.26
Calcium (mg/dl)	11.39±1.39	11.38±1.69	11.98±1.36	11.59±1.96	12.98±1.99	11.99±1.69
Magnesium (mg/dl)	2.79±0.56	2.69±0.76	2.36±0.18	2.99±0.91	2.75±0.63	2.89±0.66
Phosphorus (mg/dl)	4.98±0.99	4.79±0.65	4.69±0.39	4.96±0.23	4.87±0.28	4.72±0.29
Glucose (mg/dl)	87.94±3.92	84.64±2.98	271.4±22.3*	189±11.36*	89±2.77	84.75±2.25

\*P<0.05; <sup>#</sup>Treatment was given with diazepam 0.5 mg/kg, xylazine 0.1-0.2 mg/kg im, B-Complex 10 ml i/m and 5-10 ml of 10 % dextrose solution i/v

**Table.2** Haematological profile in Malnad Gidda cattle affected with *Anamirta cocculus* toxicity (Mean±SEM)

Group	Healthy Malnad Gidda cattle (n=6)	Malnad Gidda cattle with toxicity (n=5)	Reference values
RBCs (10 <sup>6</sup> /μl)	7.89 ± 1.97	7.98 ± 0.64	5.0-10.0
Hb (g/dl)	12.56 ± 0.96	12.97±0.63	8-15
PCV (%)	35.18 ± 2.63	34.29±0.96	24-46
MCV (fl)	48.19 ± 5.45	45.36 ± 5.81	40-60
MCH (pg)	14.19 ± 2.4	14.40 ± 3.28	11-17
WBCs (10 <sup>3</sup> /μl)	11.58 ± 1.56	12.63 ± 4.98	4.0-12.0
Platelets (10 <sup>3</sup> /μl)	296.54 ± 68.97	264.29 ± 49.87	100-800
Lymphocytes (%)	61.98 ± 4.56	56.48 ± 4.63	62-63
Neutrophils (%)	31.83 ± 5.46	40.78 ± 1.89	15-33
Eosinophils (%)	12.34 ± 0.68	11.87 ± 0.98	0-20
Monocytes (%)	6.15 ± 0.78	5.79 ± 2.21	0-8

The values are expressed as Mean±SEM.

RBCs, Red blood cells; Hb, Hemoglobin; PCV, Packed cell volume; MCV, Mean corpuscles volume; MCH, Mean corpuscles hemoglobin; WBCs, White blood cells.



**Figure.1** *Anamirta cocculus* plant



**Figure.2** *Anamirta cocculus* fruit berries



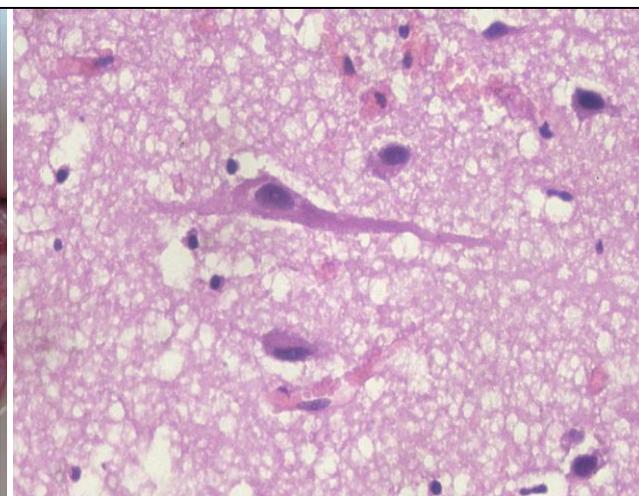
**Figure.3** Clinical signs of *Anamirta cocculus* in Malnad Gidda cattle in excited stage



**Figure.4** Recovered Malnad Gidda cattle suffered from toxicity of *Anamirta cocculus*



**Figure.5** Petechial and extensive hemorrhages in the brain of Malnad Gidda cattle died due to toxicity of *Anamirta cocculus*



**Figure.6** Section of brain of Malnad Gidda cattle died due to *Anamirta cocculus* toxicity with multifocal to diffuse vacuolations, vascular congestion, occasional haemorrhages and edema observed (H&E, 100x)

The brain histological findings were degenerative changes in the neurons and glial cells, vacuolation and myelin degeneration with structural alterations in axosomatic and axodendritic synapses. Similar type of the brain change was also observed in *Ficus ingens* toxicity in cattle indicating the neurotoxic nature of the picrotoxin ( Myburgh *et al.*, 1994).

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