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Therapeutic Management of Toxicity of *Ficus tsjahela* Leaves in Cattle

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Abstract

The toxicity episodes of *Ficus tsjahela* leaves cattle and treatment regimen were studied. The clinical signs in *Ficus tsjahela* toxicity were salivation, generalized clonic and tonic seizures, nystagmus, stereotypic gnawing behavior, hyperesthesia, ataxia, paddling movements while in recumbency and stereotyped gnawing behavior or eating inanimate objects. The affected animals were treated effectively with diazepam @ 0.5 mg/kg i/v and thiamine hydrochloride @ 10 mg/kg i/m with intravenous administration of 5-10 ml/kg of 10 % dextrose solution twice at 10 to 12 h interval for 3-4 days till complete recovery. There was no change in serum concentrations of ALT, AST, BUN, creatinine, calcium, magnesium, phosphorus except acute hyperglycemia. The phytochemical analysis revealed the presence of steroids, terpenes, diterpenes, lactones, flavonoids, tannins and glycosides. The results of this study demonstrated the toxicity of *Ficus tsjahela* leaves in cattle and its therapeutic management with diazepam, thiamine hydrochloride and dextrose.

Keywords: *Ficus tsjahela*, Toxicity, Cattle, Treatment, Diazepam, Thiamine, Dextrose.

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Introduction

Plant toxicity is also one of the cause of the death in ruminates in different parts of Karnataka. Many of such toxicities were unknown. The clinical signs exhibited by the toxicity was being confused with conditions like trypanosomiasis, hypomagnesaemia tetany and meningitis etc and was treated accordingly. But it is now well established that such clinical signs exhibited by the animals could be attributed to *Ficus tsjahela* toxicity[1,2]. *Ficus tsjahela* is distributed in Southern, Western Ghat of India and Sri Lanka and is a poisonous plant[3].

In Kannada it is called as "Kari Basari" (Figure 1 and 2). *Ficus tsjahela* is a poisonous to cattle and ingestion of this plant appeared to cause serious illness and mortality in cattle and other ruminants in Western Ghats of Karnataka, Kerala and Maharashtra[4]. Many plants said to be the fodder of cattle have proved to be toxic in higher quantity[5]. The therapy for the animals suffering from this plant toxicity was non specific and many animals were dying. The data on biochemical changes was also lacking in the suffering animals. Hence, the present study was aimed to evaluate the toxic feature of *Ficus tsjahela* in cattle, to study the biochemical changes and also to evaluate the effectiveness of treatment.

Case report

Present case study was conducted in 18 adult non-descriptive cattle which were suffering from plant toxicity as per the history of accidental feeding of the leaves of the plant *Ficus tsjahela*. The plant was botanically identified as *Ficus tsjahela* (Figure 1 and 2).

The initial clinical signs observed were salivation and excitement. As the time advanced, there was continuous twitching of palpebral muscles. Affected animals exhibited the clinical signs of hyperesthesia, frequent jaw movements, restlessness, anxious look, stereotypic gnawing behavior and erected ears. Few animals exhibited the clinical signs showed generalized clonic and tonic seizures with gnawing behavior

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Figure 1: Ficus tsjahela leaves



Figure 2: Ficus tsjahela tree

in terms of ingestion of animate (its own skin) or inanimate objects. The observed gait was abnormal with ataxia, causing in coordination during the movement of limbs and the body. Opisthotonus was the characteristic abnormality in dorsal and caudal extension of head and neck, rigid extension of hind limbs and flexion of forelimbs which was accompanied by dog sitting posture with abducted, caudally extended hind limbs and finally animals were off feed and refused to take feed and water. There was no bellowing and attacking behavior unlike rabies (Figure 3 and 4).

The rectal temperature, respiration and heart rate were recorded in regular intervals. Blood sample was collected from jugular vein at intervals of 24, 48, 72 and 96 h after onset of the *Ficus tsjahela* toxicity and before the initiation of treatment. Affected animals were treated with diazepam @ 0.5 mg/kg i/v, thiamine hydrochloride @ 10 mg/kg i/m followed by intravenous administration of 5-10 ml/kg of 10 % dextrose solution twice at 10 to 12 h interval. Serum ALT, AST, BUN, creatinine, calcium, magnesium, phosphorus and glucose concentrations were estimated and statistically analyzed.

Postmortem of two animals succumbed to the toxicity was conducted. The gross lesions were observed and the tissues from brain, liver, kidney, heart, spleen, intestine, rumen and abomasums were collected and were subjected to histological examination.

Discussion

Clinical signs observed in *Ficus tsjahela* toxicity in affected were anorexia, salivation, excitement, continuous twitching of palpebral muscles, hyperaesthesia, frequent jaw movements, restlessness, anxious look, stereotypic gnawing behavior, erected ears, ataxia, opisthotonus and dog sitting posture. Similar type of clinical signs was observed in calves fed with *Ficus tsiela* a plant belonging to same family affected calves which showed clonic and tonic seizures [6,7].

In the present study, all the affected animals were treated with diazepam @ 0.5 mg/kg, i/v, thiamine hydrochloride @ 10 mg/kg i/m followed by slow intravenous administration of 5-10 ml/kg of 10 % dextrose solution. The clinical signs were subsided gradually. After 48 h of the therapy, there was improvement in the condition, animals started taking small quantity of feed and water. Animals treated were apparently normal by fourth day and had normal rectal temperature, respiration and heart rate. Intake of fodder and water became normal, animals passed the dung of normal consistency and normal urine. However, in few animals, clinical signs re-occurred 10 to 12 h after the initial treatment and the same treatment was repeated once again. This which might be attributed to the short half life of diazepam and also the presence of the phytotoxin in the blood of the affected animal.

The clinical signs manifested by consumption of *Ficus tsjahela* leaves were of clonic-tonic seizures suggesting the neurotoxicity of this plant material. The stimulation of cerebral cortex, limbic system, cerebellum and spinal cord were implicated in genesis of clonic and tonic seizures [8]. Diazepam is a benzodiazepine is proved to be effective in treatment of seizure disorders. Intravenous diazepam or lorazepam are first-line treatments for status epilepticus. Diazepam is a drug used for the short-term treatment of epilepsy. It is the one of the easily available anti epileptic drug compared to other preparations. It is also a good sedative and do have anti anxiety property. In *Ficus tsjahela* toxicity, there will be hyperaesthesia, anxiety, excitement followed by convulsion. Hence, the clinical signs might have b subsided [9].

In the present study, diazepam @ 0.5 mg/kg i/v was given at 10 to 12 h interval. This interval schedule successfully terminated the recurrence of seizures in the cattle affected with *Ficus tsjahela* leaf toxicity. Diazepam is being studied for its sedative and appetite stimulating effects in cattle, potentiates GABA mediated inhibition on brain stem and induces sedation in cattle. Although, there is no report on the therapeutic response for the given therapy at 10 to 12 hours interval, the dose interval appeared to be ideal [10,11].

Thiamine, also known as thiamin or vitamin B_1, is a vitamin found in food and used as a dietary supplement. Thiamine is in the B complex family. It is needed for the metabolism of carbohydrates. It is proved to be effective in CNS disorders and reverses the damages to the neurons[12]. Thiamine is a cofactor for enzymes in carbohydrate metabolism and forms thiamine pyrophosphate, which is involved in carbohydrate metabolism and produces energy. Thiamine deficiency affects carbohydrate metabolism and disorder in ruminants includes listlessness, circling movements, opisthotonus and muscle tremors. Hence in the present study, thiamine hydrochloride @ 10 mg/kg, i/m followed by intravenous administration of 5-10 ml/kg of 10 % dextrose solution to meet the energy requirement of the animals affected with *Ficus tsjahela* leaves toxicity[13].

Table 1. Biochemical profile in healthy and *F. tsjahela* toxicity observed cattle (mean±SE)

Parameter	Apparently healthy cattle (n=10)	Cattle affected with *F. tsjahela* toxicity (n=18)				
		0 hour	24 hours#	48 hours#	72 hours	96 hours
Alanine amino Transferase (ALT in U/L)	27.5±2.10	29.27±1.89	27.68±2.76	29.30±1.73	28.53±1.24	27.82±2.53
Aspartate amino Transferase (AST in U/L)	56.2±2.5	57.67±1.98	56.97±2.06	57.33±2.97	56.83±1.49	58.48±1.54
Blood Urea Nitrogen (BUN in U/L)	18.90±1.61	20.38±1.63	21.15±0.26	19.10±1.39	17.42±1.57	19.00±1.08
Creatinine (mg/dl)	1.13±0.20	1.30±0.20	1.23±0.30	1.31±0.24	1.10±0.20	1.18±0.20
Calcium (mg/dl)	11.3±1.30	10.37±1.29	10.03±1.24	10.20±1.21	11.04±1.19	11.12±1.24
Magnesium (mg/dl)	2.60±0.15	2.58±0.16	2.38±0.17	2.42±0.18	2.52±0.11	2.40±0.13
Phosphorus (mg/dl)	4.90±0.30	4.70±0.27	4.73±0.31	4.80±0.23	4.60±0.21	4.66±0.20
Glucose (mg/dl)	78±2.70	75.50±2.40	261±21.20*	141±10.70*	99±2.27*	85±2.43

*P<0.05

#Treatment was given with diazepam 0.5 mg/kg bw i/v, thiamine hydrochloride 10 mg/kg, i/m followed by 5-10 ml of 10 % dextrose solution i/v.



Figure 3: Clinical signs of Ficus tsjahela toxicity in cross bred calf



Figure 4: Clinical signs of Ficus tsjahela toxicity in Malenadu Gidda cow

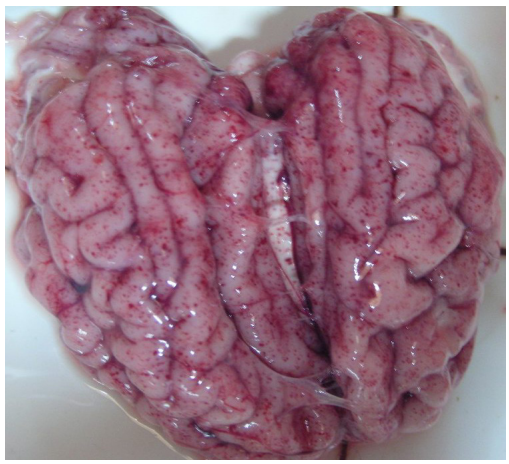


Figure 5: Petecchial and extensive hemorrhages in the brain of cow died due to toxicity of Ficus tsjahela

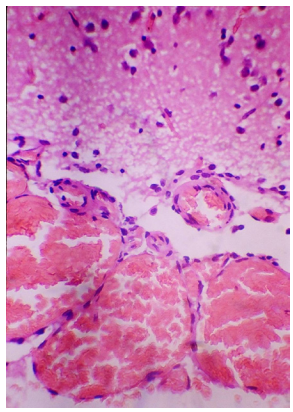


Figure 6: Section of brain of cow affected with Ficus tsjahela toxicity showing prominent congestion of meningeal blood vessels

There was no change in the concentrations of ALT, AST, BUN, creatinine, calcium, magnesium, phosphorus but there was significant (P< 0.05) hyperglycemia (Table 1). Except for hyperglycemia noticed after convulsions, there was no significant change (P>0.05) in calcium, magnesium and phosphorus. Hyperglycemia could be attributed to muscle tremors, hyperactivity of muscles resulted in glycogenolysis. Along with the neurological signs, it was observed that, there was increased blood glucose level in cross-bred male calves fed with *Ficus tsjahela* leaves which might be associated with excessive muscle contractions. The observed acute hyperglycemia after the occurrence of seizures, suggested the possibility of hyperglycemia to the seizures [14,15,16,17].

In the present study, there was extensive hemorrhages in the brain of the affected animals. There were degenerative changes in the neurons and glial cells (Figure 5 and 6). This finding is in according to the findings observed in an experimental toxicity of *Ficus tsiela* leaves which was induced in cross-bred calves where in neurological signs were observed. There was ultrastructural change in brain like degenerative changes in the neurons and glial cells, vacuolation and myelin degeneration with structural alterations in axosomatic and axodendritic synapses [18,19].

The phytochemical analysis revealed the presence of steroids, terpenes, diterpenes, lactones, flavonoids, tannins and glycosides. Study revealed that the latex of the plant do induce the toxicity which might have more neurotoxic phytotoxin in it in high quantity. Similarly, leaves of *Ficus tsiela*, another similar plant were extracted with different solvents and evaluated the phytochemical analysis. The presence of biological constituents namely terpenoids, tannins, steroids, anthraquinones, flavonoids, saponins, cardiac glycosides and phlobatannin were confirmed through preliminary phytochemical analysis [19].

Further studies are required on isolated chemical constituents of *Ficus tsjahela* in cattle as well as other laboratory to assess the toxicity of each chemical constituent. There is necessary to find a good remedial measure with a good anti epileptic and anti anxiety drug with long half life, good safety with ease of availability is also necessary.

Conclusion

The present study evaluated the efficacy of treatment in the toxicity of *Ficus tsjahela* leaves in cattle. The clinical signs in *Ficus tsjahela* toxicity were salivation, generalized clonic and tonic seizures, nystagmus, stereotypic gnawing behavior, hyperaesthesia, ataxia, paddling movements while in recumbency and stereotyped gnawing behavior or eating inanimate objects. The affected animals were treated effectively with diazepam @ 0.5 mg/kg i/v and thiamine hydrochloride @ 10 mg/kg i/m with intravenous administration of 5-10 ml/kg of 10% dextrose solution twice at 10 to 12 h interval. There was no change in serum concentrations of ALT, AST, BUN, creatinine, calcium, magnesium, phosphorus except acute hyperglycemia. The phytochemical analysis revealed the presence of steroids, terpenes, diterpenes, lactones, flavonoids, tannins and glycosides. The results of this study demonstrated the toxicity of *F. tsjahela* leaves in cattle and its management with diazepam, thiamine hydrochloride and dextrose.

Conflict of interest

No conflict of interest.

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References

1. Shridhar, N.B., Toxicity of *Ficus tsjahela* leaves in cattle and its treatment http://www.ivis.org/proceedings/wbc/2010/AbstractCD/OP-PO02q.htm
2. Shridhar, N. B., Krishna, N. S. and Santhosh Kumar, C. N. Toxicity of *Ficus Tsjahela* leaves in cattle and its clinical management. Indian Vet.J., 2014;91(7) 49-50.
3. Yoganarasimhan, S.N., Subramanium, K. and Razi, B.A. Flora *of* Chikkamagalur District. Karnataka, India, International Book Distributors, Dehradun, 1981; 308-309.
4. Narayana, K., Pradeep, S.K., Usha, N. and Shridhar, N.B. (2003) Moraceae, In: Poisonous and Medical Plants. 1st ed. Jayashree Publications, Bangalore, pp. 17-18.
5. Chanda, S.K. and Bhaid, M.U. Studies on the digestibility and nutritive value of common dried fodder tree leaves of M.P. on goats: 4. Hay of phephar tree leaves (*Ficus tsiela* Roxb). Livest. Advis.,1987;12, 5-8.
6. Nair, N.D., Abraham, M.J., Valsala, K.V., Nair, M.G. and Rajan, A. Clinico-patho logical features of experimental chela leaf poisoning in calves. Kerala J. Vet. Sci., 1987;18, 84-90.
7. Rajan, A., Nair, N.D., Valsala, K.V., Maryamma, K.I. and Ramachandran, K.M. Pathology of a nervous disorder in

cattle caused by the toxicity of leaves of the tree *Ficus tsiela* Roxb. Indian Vet. J.,1986; 63,184-186.
8. Rodostists, O.M., Blood, D.C. and Gay, C.C. Diseases of nervous System. In: *Veterinary Medicine*. 8th ed. E.L.B.S, London, 1994; 458-503.
9. Riss, J., Cloyd, J., Gates, J. and Collins, S. Benzodiazepines in epilepsy: Pharmacology and pharmacokinetics. Acta Neurologica Scandinavica, 2008; 118 (2)69–86.
10. Booth, N.H. and McDonald, L.E. Psychotropic agents. In: *Veterinary Pharmacology and Therapeutics,* 6th ed. Panima Publishing Corporation, New Delhi, 1998; 363-395.
11. Krishna, N.S. Toxicity studies of *Ficus tsjhela* in cattle. M.V.Sc. Thesis submitted to University of Agricultural Sciences, Bengaluru, 1999.
12. Bettendorff, L., Mastrogiacomo, F., Kish, S. J. and Grisar, T. Thiamine, thiamine phosphates and their metabolizing enzymes in human brain. *J. Neurochem*., 1996; 66 (1) 250–258.
13. Tolga, K., Murat, D. and Omer, K. Thiamine status of feedlot cattle fed a high-concentrate diet. *Can. Vet. J.*, 2010; 51(11): 1251–1253.
14. Ratnasooriya, W.D., Premakumar, G.A.S. and Tillekeratne, L.M.V. Exploratory behaviour of male rats treated with a crude extract of *Ficus tsiela* leaves. Med. Sci. Res.,1992; 20, 233-234.
15. Geetha, B.S., Mathew, B.C. and Augusti, K.T. (1994). Hypoglycemic effects of leucodelphinidin derivative isolated from *Ficus bengalensis* (Linn). Indian J. Physiol. Pharmacol.,1994; 38, 220-222.
16. Bafor, E.E and Igbinuwen, O. Acute toxicity studies of the leaf extract of Ficus exasperata on haematological parameters, body weight and body temperature. J. Ethnopharmacol., 2009; 123(2):302-307.
17. Litty Mathew, Divakaran Nair, N., Vijayan, N. and Mercey, K. A. Hemato-biochemical and oxidative effect of fresh juice and ethanolic extract of *Ficus tsiela* Roxb in rats. Vet. World, 2014; 7(10) 890-894.
18. Nair, N.D., Rajan, A. and Nair, M.K. Histopathology of toxicity of *Ficus tsiela* in cattle (1995) *Indian J. Vet. Pathol.*, **19**: 1-5.
19. Myburgh, J.G., Fourie, N. Van der Lugt, J.J., Kellerman, T.S., Cornelius S, T., Ward, C. A nervous disorder in cattle, caused by the plants *Ficus ingens* var. *ingens* and *Ficus cordata* subsp. *salicifolia*. Onderstepoort J. Vet. Res., 1994; 61(2)171-6.
20. Ramesh K. Satdive, Raghuram Chimata, Ajay Namdeo and Devanand, P. Fulzele. *In vitro* screening for phytochemical and antimicrobial activity of poisonous plant *Ficus Tseila* Roxb. Int. J. Pharma Bio. Sci., 2012; 3(2) 213-221.