Journal of Entomology and Zoology Studies

Available online at www.entomoljournal.com

E-ISSN: 2320-7078
P-ISSN: 2349-6800
www.entomoljournal.com
JEZS 2020; 8(3): 1774-1776

Received: 01-03-2020
Accepted: 03-04-2020

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Evaluation of acute oral toxicity of a polyherbal dam and calf care formulation in Swiss albino mice

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Abstract
The current study was designed to evaluate the acute oral toxicity potential of AV/MCC/18 (M/s Ayurvet Limited, Baddi, India) according to OECD 423 guidelines. AV/MCC/18 is a dam and calf care formula for preparturient livestock. Nine female Swiss albino mice were used for the study. Each animal served as its own control. Following the oral administration of the test substance, the animals were observed for manifestation of toxic effects and deaths. No toxic effects or mortalities were observed. The estimation of biochemical parameters (AST, ALT, ALP and Creatinine) and histopathological studies also did not reveal any significant findings. Hence, AV/MCC/18 was found to be safe for use.

Keywords: Acute oral toxicity, AV/MCC/18, OECD 423, safety

Introduction
Continuous selection of dairy cows for increased output over the past several years has led to changes in their ability to meet increased energy and protein demands, partially responsible for a decline in their reproductive efficiency. Levels of dietary energy intake can influence the expression of gene transcripts in the embryo and optimum levels are required for healthy conception, implantation, blastocyst formation and early embryonic development [1]. Insufficient maternal nutrition may lead to impaired fetal development, abortions, dystokia and congenital anomalies [2]. Immunological defense in female reproductive tract should be sufficient to prevent conceptus rejection owing to its foreign nature and microbial colonization [3]. Maternal nutrition plays an important role to potentiate the immune response and sustain pregnancy [4]. AV/MCC/18 is a polyherbal formulation for dam and calf care during the preparturient period. Herbs like *Asparagus racemosus*, *Withania somnifera*, *Tinospora cordifolia* and *Cynodon dactylon*, make AV/MCC/18 an ideal supplement for promoting early conception, placentation and implantation [5], for fetal-maternal nourishment, fetal growth and development, for reducing incidences of abortions, dystokia and congenital anomalies; and for alleviating gestational stress.[6] AV/MCC/18 supplementation significantly reduces the number of services for successful conception, increases the number as well as birth weight of the piglets and reduces the mortality in the newborn [7]. In buffaloes, it has been shown to qualitatively and quantitatively improve milk parameters and sustain the productive potential of second or third parity buffaloes during early to mid lactation [8]. The present study aimed at determining the acute oral toxicity potential of AV/MCC/18.

Materials and Methods
The animals for the current study were procured from CPCSEA-registered breeding source *viz.* laboratory animal resource section of Department of Pharmacology and Toxicology, PGIVAS, Akola. Nine healthy, adult, nulliparous and non-pregnant female Swiss albino mice (20-25g) were used. Animals were kept in the cages for five days for acclimatization. The animals were fasted over-night, food but not water was withheld for 3-4 hours. Following the period of fasting, the animals were weighed and the test substance was administered orally. The animals were identified by appropriate means. The number of animals per cage was kept at three for clear observation of each animal; housing conditions were conventional. The ambient temperature was 25 °C and relative humidity was 70%. The animals were exposed to 12 hour light-dark cycle and provided with standard pelleted diet and water *ad lib* [9].

After the administration of the test substance @ 300 mg/Kg (P.O.) in normal saline and 2000 mg/Kg with maximum volume 2 mL/ 100 g body weight, food was withheld for 1-2 hours. The animals were observed intensively for 24 h, and then for further 14 days for manifestation of toxic effects and deaths; LD_{50} value was also estimated. The observations included changes in skin, fur and eyes; and changes in respiratory, circulatory, CNS, autonomic, somatic activity and behavior. Clinical signs like muscular tremors, convulsions, salivation, diarrhea, lethargy, sleep, and coma, if any, observed during study period were recorded.

Results

Individual body weights of mice were recorded on days 0, 7 and 14 of the study and body weights in both the groups (I and II) continued to increase throughout the study period (Table 1).

Table 1: Individual body weights of experimental mice

Formulation and Dose	Mice No.	Body Weight (g) on Day		
		0	7	14
AV/MCC/18 @ 300 mg/Kg b.wt. orally (Group I)	1	23	24	26
	2	20	22	24
	3	21	23	25
	Mean±SE	21.33±1.11	23.00±0.73	25.00±0.73
AV/MCC/18 @ 2000 mg/Kg b.wt. orally (Group II)	1	21	23	25
	2	25	26	27
	3	20	22	24
	4	21	23	25
	5	25	25	27
	6	21	22	25
	Mean±SE	22.17±0.91	23.50±0.67	25.50±0.50

No mortality was observed throughout the period of observation. In the six mice receiving the limit dose of AV/MCC/18 at 2000 mg/Kg, *i.e.* the maximum dose which can be administered by oral route, no mortality occurred and hence, the LD_{50} was beyond this limit. Similarly, no abnormal symptoms, including lethargy, tremor, abdominal breathing, piloerection were observed up to 14 days of AV/MCC/18 administration. Necropsy on day 14 did not show any remarkable findings in the gross or microscopic appearance of liver, kidney, spleen, heart, lungs, and genital organs in any of the animals. Pooled serum samples were analyzed in triplicate for AST, ALT, ALP and creatinine and all were within their normal ranges (Table 2).

Table 2: Biochemical findings in experimental mice

Dose	AST (IU/L)	ALT (IU/L)	ALP (IU/L)	Creatinine (mg/dL)
300 mg/Kg	58.8	13.76	28.16	0.52
2000 mg/Kg	62.96	15.06	37.33	0.25

Discussion

AV/MCC/18 contains herbs like *Asparagus racemosus*, *Withania somnifera*, *Tinospora cordifolia* and *Cynodon dactylon*, that fall under the category of Generally Regarded As Safe (GRAS). A composition based on these GRAS constituents is least likely to be toxic in practical doses. Due to the presence of multiple active ingredients, AV/MCC/18 exerts multifarious benefits on cattle and livestock, including uterine strengthening, feto-maternal nourishment, averting abortion, and augmentation of fetal growth.

Conclusion

AV/MCC/18 did not produce acute oral toxicity, evident as absence of mortality or any toxic clinical symptoms, when administered up to limit dose (2000 mg/Kg) in mice. Based on this study, the formulation was found safe for oral use.

Acknowledgment

The authors acknowledge M/s Ayurvet Limited for funding the study.

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