Original Research Article

Acute oral toxicity of a herbal gut function modulator

ABSTRACT:

The current study was designed to evaluate the acute oral toxicity potential of AV/AGP/30 (M/s Ayurvet Limited, Baddi, India) according to OECD 423 guidelines. AV/AGP/30 is a polyherbal gut function modulator in swine and poultry. 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/AGP/30 was found to be safe for use.

Keywords: Acute oral toxicity, AV/AGP/30, OECD 423, safety, limit test

INTRODUCTION:

Improving gut function is key to profitability in livestock enterprises because up to 60% of total costs are incurred on feeding [1]. The gut also plays extremely important roles as an immunity and endocrine organ. The manipulation of gut microbiota greatly affects body composition and host metabolism. Also, gut microbiome exerts a marked influence on host physiology [2]. Restrictions on the use of antibiotics as growth promoters are seeing the increased use of herbal gut function modulators in different species of livestock [3], especially so, in poultry and pigs, which are reared under relatively higher magnitudes of production stress and hence, more vulnerable to diseases.

AV/AGP/30 is a herbal gut function modulator for use in poultry and swine. It is recommended for inhibition of pathogenic bacteria, for promoting intestinal microbio-cenosis, and for the improvement of gastrointestinal health, growth performance and feed efficiency. AV/AGP/30 is highly effective at stabilizing gut mucosa and, thus, reduces incidences of diarrhea and enteritis.

In a study comparing its efficacy with the antibiotic Bacitracin Methylene Disalicylate (BMD), AV/AGP/30 was found superior to BMD at improving growth, performance and FCR, resulting in higher Broiler Performance Efficiency Index (BFEI) and profitability. Supplementation with AV/AGP/30 resulted in better intestinal histomorphology, which may be posited as the primary mechanism for its activity [4]. The present study was undertaken to ascertain the efficacy of AV/AGP/30 as gut function modulator.

MATERIALS & 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 (20-25 g) were used. Animals were kept in the cages for five days for acclimatization. The animals were fasted over-night, food but not water 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 of 70%. The animals were exposed to 12 hour light-dark cycle and provided with standard pelleted diet and water *ad lib* [5].

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 for 24 h, 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 weight of mice was recorded on days 0, 7 and 14 of the study and body weight of 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/AGP/30@ 300 mg/Kg b.wt. orally (Group I)	1	20	22	23
	2	21	23	24
	3	20	22	24
	Mean ± SE	20.33±0.57	22.33±0.57	23.66±0.57
AV/AGP/30@ 2000 mg/Kg b.wt. orally (Group II)	1	20	21	24
	2	20	22	25
	3	21	22	24
	4	21	23	25
	5	21	23	25
	6	20	22	24
	Mean ± SE	20.50±0.54	22.16±0.75	24.5±0.54

No mortality was observed throughout the period of observation. In the six mice receiving the limit dose of AV/AGP/30 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/AGP/30 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	68.96	38.8	92.66	0.68
2000 mg/Kg	94.03	42.43	97.03	0.60

DISCUSSION AND CONCLUSION:

AV/AGP/30 is a herbal formulation, containing ingredients 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. AV/AGP/30 did not produce acute oral toxicity, evident as absence of mortality or any toxic clinical symptoms, when administered up to limit dose (2000mg/Kg) in mice. Based on this study, the formulation was found safe for oral use.

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