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Therapeutic potential of doramectin against canine sacroptic mange

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Abstract
Present study describes the haemato-biochemical analysis of dogs affected with sarcoptic mange and its treatment using doramectin. Study was undertaken on six client owned dogs confirmed to be suffering from sarcoptic mange irrespective of age, sex and breed presented at TVCC DUVASU, Mathura, while six healthy dogs were taken as control. There was significantly higher concentration of haematological parameters viz. total leucocyte count, eosinophil counts, mean corpuscular volume in scabetic dogs than respective control animals. On contrary mean concentration of haemoglobin, total erythrocyte count, haematocrit, lymphocyte counts decreased significantly in scabetic dogs than respective control animals. The biochemical parameters revealed significantly higher concentration of aspartate aminotransferase and alanine aminotransferase (30.14±0.60 µ/L vs 21.49±1.20 µ/L, 38.01±1.02 µ/L vs 28.33±3.72 µ/L; respectively) in scabetic dogs than in control while significant lower concentration of glucose, cholesterol, total protein and albumin in scabetic dogs than in control (46.83±1.57 mg/dL vs 70.33±3.16 mg/dL, 164.50±5.15 mg/dL vs 222.83±11.89 mg/dL, 4.46±0.11 gm/dL vs 6.06±0.06 gm/dL and 1.70±0.06 gm/dL vs 3.21±0.06 gm/dL; respectively). Cases were efficiently managed by using subcutaneous injections of doramectin @ 0.4 mg/kg body weight subcutaneously at weekly intervals along with standard treatment of pyoderma.

Keywords: *Sarcoptes scabiei*: doramectin

1. Introduction
Dermatological ailments are frequently encountered in the small animal practice especially in the tropical countries like India. It has been estimated that between 20% to 75% of the small animals have skin problems as a chief or concurrent complaint [1]. Among these skin problems, parasitic mites are clinically very important as only genus *Sarcoptes* mayinfest up to 40 different mammalian hosts across 17 families [2]. Canine scabies is an intensely pruritic, non-seasonal, transmissible canine dermatosis caused by infestation with the epidermal mite *Sarcoptes scabiei var. canis* [3, 4]. It is the most common pruritic zoonosis as 50% of human cases may result due to handling of the infected dogs [5]. The disease is characterized by severe pruritic papular eruptions, pinpoint crusts in combination with alopecia [6, 7] lead by secondary self-inflicted traumatic excoriations. Skin lesions have a focal to multifocal distribution and are characterized by varying degrees of crusting and alopecia depending on the species and individual [8]. Typically, lesions are observed on the head and the pinnae, the legs (particularly the elbows and the hocks) and the ventrum [9, 10] however dorsum of the trunk remains relatively spared. Small blisters may open and become covered with scab or by plaques that may often ooze fluid. Skin may become thickened and wrinkled, with cracks and fissures with heavy dandruff evident on hairy areas covering the neck and abdominal region [11]. Most of the clinical features (including intense pruritus) that characterize sarcoptic mange in all the species are most likely associated with hypersensitivity reaction [12] to various mite antigens including protein in the cuticle and the faeces. Secondary pyoderma and consequent septicaemia and death may occur in few cases [13, 14]. Haematological picture in affected dog includes lower erythrocytes count, packed cell volume, haemoglobin [15] and increased total leukocyte count with neutrophilia [16]. Barring other pathological changes, decrease in digestibility of feed, absorption of nutrient and alteration in hepatic structure and function occurs [17, 18]. Macrocyclic lactones (avermectins and milbemycins) are broad-spectrum antiparasitic drugs widely used for the treatment of various parasitic ailments in veterinary medicine. Doramectin

is an avermectin with a prolonged activity and plasma half-life compared with ivermectin [19]. According to Jagannath and Yathiraj [20] a single dose of 0.2 mg / kg of intramuscular or subcutaneous doramectin was sufficient to treat sarcoptic mange in 23 dogs studied, without the occurrence of side effects and with good tolerance even for puppies. Hence the present study was conducted to evaluate the therapeutic potential of doramectin against canine sarcoptic mange infestation.

Materials and Methods

Selection of dogs

The present study was undertaken on six client owned dogs confirmed to be suffering from sarcoptic mange irrespective of age, sex and breed presented at TVCC, DUVASU, Mathura, while six healthy dogs were taken as control. The most prominent clinical signs observed were persistent and intense pruritus, alopecia, crustformations, excoriations and irritability in all clinical cases. The lesions were observed on head, pinnae, legs (elbows and hocks) and ventrum. Confirmation of sarcoptic mange was based on the presence of *Sarcoptes scabiei* mites or mites with their developmental stages on microscopic examination. Fecal samples were negative for eggs of internal parasites and dogs were free from any concurrent disease in study group.

Collection of blood

With the informed oral consent of the dog owners, about 5 ml of blood from each diseased animal was collected from the recurrent tarsal or radial vein using disposable syringe and needleat 0, 14 and 28 days interval during the study period.Instantly after collection, 2 ml of blood was transferred into vials containing EDTA for assays of haematological panels. Remaining 3 ml of blood was taken in plane vials without any anticoagulant and the vials were kept in a slanted position for 25-30 minutes at normal room temperature, followed by subjected to be centrifuged @2000 rpm for 5 minutes for harvesting of serum for the study of biochemical panels. Similarly blood samples were also procured from the healthy dogs and were used as reference value (Control Group).

Mite counts

For parasitological examination, a dulled scalpel blade was held perpendicular to the skin and used with modest pressure to scrape in the direction of hair growth. Skin scraping samples of 5 cm×5 cm were taken from five affected sites. Scraping samples of the dogs from the study group were transferred into test tube, and 2-3 ml of 10% KOH was added; samples were mildly heated over spirit lamp until for 1–2 bumps were seen and then centrifuged on 1500 rpm for 5 min. Obtained precipitates were examined under microscope, and mites were identified according to morphological features. The average mite count was determined by averaging the mite count from five fields and was performed on days 0, 14 and 28 to assess the laboratory-based recovery (Parasitological cure).

Treatment

Dogs with sarcoptic acariasis were treated with Inj. Doramectin @ 0.4 mg/kg b.wt. SC every week for 5 treatments [21] along with standard treatment of pyoderma if any with Tab. Cephalexin @ 15-20 mg/kg b.wt. bid PO for 7-10 days and Shampoo containing chlorhexidine gluconate 2.1% and ketoconazole 1% applied at weekly intervals.

Statistical analysis

The values of various parameters were expressed as mean ± S.E. and Data were analysed by one-way (ANOVA) Analysis of Variance followed by the Post-Hoc tukey HSD test using Statistical Package for the Social Sciences (SPSS 16.0). The level of statistical significance for all comparisons was established at ($P<0.05$).

Results and Discussion

The mean values of haemato-biochemical parameters viz. total leucocyte count, eosinophil counts, mean corpuscular volume, aspartate aminotransferase, alanine aminotransferase were significantly higher in scabetic dogs than in control while haemoglobin, total erythrocyte count, haematocrit, lymphocyte counts, glucose, cholesterol total protein, albumin, albumin/globulin ratio and blood urea nitrogen showed significantly lower mean values in scabetic dogs than in control. Significant amelioration in various haematological and biochemical parameters were recorded on day 28 post therapy in the treatment group. However, biochemical parameters like AST, ALT and cholesterol levels could not attain comparable values to that of healthy controls at day 28 post therapy in treatment group. The parasitological cure rate was calculated as the proportion of dogs negative for *S. scabiei* mites on the basis of microscopic examination of deep skin scrapings obtained on day 14 and 28 post therapy. In Sarcoptes-infested dogs, the parasitological cure rate on day 14 and 28 post therapy was 40% and 100% respectively.

Haematology

Table 1 depicts alteration in the haematological parameters before and after treatment. In the present study the sarcoptic mange affected dogs had significantly higher total leukocyte and eosinophils counts than control group. Observations of leucocytosis along with eosinophilia in present study is parallel with the findings of Sharma *et al*. [22], Sakina and Mandial [23], Reddy *et al*. [24], Narang *et al*. [25] and Beigh *et al*. [26]. Suggested reason of leucocytosis is the allergic reaction caused by mite or their products of inflammatory reaction [27, 28], cellular and humoral immune response [29]. Eosinophilia observed was probably because of the allergic reaction caused by mites or activation of immune system. The excretion and secretion of living mites have an irritant and allergenic effect [8]. The increased total leukocyte and eosinophils counts can be attributed to the inflammatory conditions related to disease, which becomes normal after 28th day of therapy in the treatment group. Lymphopenia was consistent finding in cases of sarcoptic mange which simulated the findings of Nair and Nauriyal [30], Behera *et al*. [31] and Sakina and Mandial [23]. It might be due to the reason that cell mediated immunity plays important role in fighting against sarcoptic mites. In present study there was significant reduction observed in HCT % at day 0 in the diseased group as compared to healthy group at day 0, which is analogous with previous findings of Behera *et al*. [31], Lodh *et al.* [32], Beigh *et al*. [33], Reddy *et al*. [24] and Beigh *et al*. [26]. Decreased levels of HCT may be due to chronicity and generalized nature of the disease [34] and erythrocyte fragility and low production of erythropoietin due to toxaemia caused by mites. The estimated panels also attained comparable values to that of healthy controls at day 28 post therapy.

Present study revealed significant reduction in Hb and TEC

values in the sarcoptic infested group in comparison to healthy group. The decrease in the values of haemoglobin and TEC is possibly due to anaemia caused by the loss of skin protein and stress arising from the disease [35-37]. Significantly declined Hb level of sarcoptic infested dogs in level of sarcoptic infested dogs in our study is parallel with previous findings of Behera *et al.* [31], Lodh *et al.* [32], Sakina and Mandial [23], Reddy *et al.* [24], Beigh *et al.* [26]. MCV values were significantly higher in dogs suffering from sarcoptic mange as compared to control group indicating macrocytic anaemia in sarcoptic dogs. Similar observations in regard to MCV in dogs suffering from sarcoptic mange were previously recorded [23]. Significant amelioration was noticed in Hb, TEC and MCV values on day 28 post therapy in the treatment group. Present study showed significantly reduction in MCH and MCHC and significantly elevation in MCV in the diseased groups as compared to healthy group. Sakina and Mandial [23] reported significantly elevated MCV and MCH levels in scabetic dogs however, Beigh *et al.* [33] reported that the mean value of MCH, MCHC & MCV in scabies infected dog do not differ significantly from control group. Increase in MCV might be due to less supply of maturation factors required for maturation of erythrocyte, due to in appetence associated with disease. Reduction in MCH and MCHC was either due to chronic and generalised nature of disease or inappetance developed for a longer period due to pruritogenic nature of mites. Marked amelioration was observed in the treatment group 28 days post therapy.

Serum biochemistry

Table 2 depicts alteration in the serum biochemical parameters before and after treatment. In the present study the mean blood glucose levels in sarcoptic dogs was significantly lower than in control indicating hypoglycaemia, which is in agreement with previous findings of Sakina and Mandial [23], Narang *et al.* [25] and Beigh *et al.* [26]. Hypoglycaemia in scabies might be due to increased need of skin, during inflammatory reactions [38]. The serum glucose level in the diseased group increased towards normalcy at day 28 post therapy. A significant decrease in mean serum total protein level in sarcoptic dogs as compared to the healthy group indicated hypoproteinaemia, which was in agreement with the observations of Biswas *et al.* [37], Solanki *et al.* [39] and Sakina and Mandial [23]. A significant decrease in mean serum albumin level in sarcoptic dogs as compared to the healthy group indicated hypoalbuminemia. Similarly, Lodh *et al.* [32] reported that the mean total serum protein and albumin of scabies infected dogs were significantly lower than that of the control group. A significant decrease in albumin-globulin ratio level in sarcoptic dogs as compared to the healthy group was also noticed in our study. In the present study, lower albumin level would have resulted in decreased total protein and A/G ratio. Similarly, Behera *et al.* [31] reported significantly decreased biochemical parameters such as total serum protein, serum albumin and A/G ratio in all infested dogs in comparison to healthy dogs. Present findings were in agreement with the earlier findings of decreased total protein and albumin in canine scabies [16] and sarcoptic mange in sheep [40]. Similar findings of decreased albumin values were also reported by Beigh *et al.* [26]. As the reduction in total serum protein was observed in affected dogs because albumin that is released leading to hypoprotinemic condition and that may be due to burrowing nature of the mite leading to leaching of protein fractions from the body fluids [41]. In the present study the decreased albumin levels might either be due to malnutrition or parasitism [42, 43, 44], which sufficiently showed that scabies affects feed conversion efficiency and growth weights. Decrease in albumin levels might be attributed to continuous loss of plasma protein through internal bleeding and subsequent haemodilution as a result of mobilization of fluid from pruritis which attributed to hypoalbuminemia [41]. The estimated panels achieved a comparable value to that of healthy animals at day 28 post therapy. In the present study nonsignificant difference in mean serum globulin level in sarcoptic dogs was recorded as compared to the healthy group, which is in agreement with the findings of Lodh *et al.* [32]. However, Sakina and Mandial [23] and Beigh *et al.* [26] recorded hyperglobinemia in sarcoptic infested dogs.

In the present study the mean AST & ALT levels in sarcoptic dogs was significantly higher than in control. Similarly, Beigh *et al.* [26] reported elevated AST & ALT level in severely scabies-infected dogs which points toward compromised liver functions. Elevated levels of ALT, AST and decreased levels of albumin, glucose and cholesterol points toward compromised liver functions in severely scabies-infected dogs. As liver is the main organ for glycogenolysis, gluconeogenesis and for albumin and cholesterol synthesis decreased glucose, albumin and cholesterol concentration observed could be attributed to decreased synthesis by the liver. Similar changes in biochemical parameters have also been observed in sarcoptic mange affected goats [45] and dogs [46]. In present study significantly decreased BUN values were recorded at day 0 & 14 in diseased dogs as compared to the values of healthy dogs, while no significant changes were observed in creatinine values. Allaam *et al.* [47] reported significantly low urea and creatinine in Egyptian Buffaloes (*Bubalusbubalis*) infested by sarcoptic mangeand attributed that decrease of urea should be linked with loss of appetite. The estimated panels attained comparable values to that of healthy controls at day 28 post therapy in both the treatment groups.

Table 1: Hematological parameters of healthy dogs and dogs suffering from Canine Sarcoptic Acariasis**.**

Groups	TLC (10^3/µL)			Granulocyte (%)			Lymphocyte (%)		
	DAY 0	DAY 14	DAY 28	DAY 0	DAY 14	DAY 28	DAY 0	DAY 14	DAY 28
Healthy	14.32 ± 0.73^{a}	14.36 ± 0.93^{a}	14.35 ± 0.94	63.16 ± 0.74^{a}	62.98 ± 1.37^{a}	62.63 ± 1.64	30.28 ± 0.74^{b}	30.45 ± 1.18^{b}	30.75 ± 1.39
Diseased	20.90 ± 0.52^{bC}	18.25 ± 0.56^{bB}	14.73 ± 0.43^{A}	88.57 ± 0.65^{bC}	77.73 ± 1.69^{bB}	64.78 ± 0.70^{A}	5.89 ± 0.39^{aA}	15.41 ± 1.64^{aB}	27.27 ± 1.90^{C}

Groups	Monocyte (%)			Eosinophil (%)			Hb (gm/dL)		
	DAY 0	DAY 14	DAY 28	DAY 0	DAY 14	DAY 28	DAY 0	DAY 14	DAY 28
Healthy	6.40 ± 0.11	6.40 ± 0.23	6.51 ± 0.30	5.16 ± 0.47^{a}	5.50 ± 0.34^{a}	5.66 ± 0.49	14.26 ± 0.57^{b}	14.21 ± 0.51^{b}	14.40 ± 0.52
Diseased	5.63 ± 0.23	5.48 ± 0.28	6.00 ± 0.62	11.16 ± 0.79^{bC}	8.66 ± 0.61^{bB}	5.83 ± 0.47^{A}	8.53 ± 0.21^{aA}	10.68 ± 0.49^{aB}	13.46 ± 0.73^{C}

Groups	HCT (%)			MCV (fL)			MCH (pg)		
	DAY 0	DAY 14	DAY 28	DAY 0	DAY 14	DAY 28	DAY 0	DAY 14	DAY 28
Healthy	41.23 ± 0.75^{b}	41.30 ± 0.73	41.71 ± 0.67	67.16 ± 0.53^{a}	68.05 ± 0.80^{a}	68.21 ± 1.01	23.16 ± 0.61^{b}	23.35 ± 0.61	23.50 ± 0.57
Diseased	37.11 ± 0.61^{aA}	39.20 ± 0.73^{B}	40.66 ± 0.45^{B}	88.91 ± 3.41^{bB}	77.7 ± 4.8^{abAB}	69.15 ± 1.5^{A}	20.33 ± 0.39^{a}	21.25 ± 1.84	22.88 ± 1.29

GROUPS	MCHC (g/dL)			TEC (10^6/µL)			PLATELET (10^3/µL)		
	DAY 0	DAY 14	DAY 28	DAY 0	DAY 14	DAY 28	DAY 0	DAY 14	DAY 28
Healthy	34.48 ± 0.78^{b}	34.31 ± 0.65^{b}	34.41 ± 0.77	6.13 ± 0.10^{b}	6.06 ± 0.11^{b}	6.11 ± 0.11	265.50 ± 12.85	265.50 ± 12.80	265.66 ± 12.94
Diseased	22.98 ± 0.75^{aA}	27.30 ± 1.60^{aA}	33.06 ± 1.79^{B}	4.19 ± 0.14^{aA}	5.12 ± 0.28^{aB}	5.89 ± 0.13^{C}	251.66 ± 9.71	255.66 ± 12.30	250.33 ± 10.60

Mean with different superscript (a, b) in columns are differing significantly in between the groups, otherwise non-significant. Mean with different superscript (A, B, C) in rows are differing significantly in between the intervals, otherwise non-significant.

Table 2: Biochemical parameters of healthy dogs and dogs suffering from Canine Sarcoptic Acariasis

Groups	Glucose (mg/dL)			Cholesterol (mg/dL)			Triglyceride (mg/dL)		
	DAY 0	DAY 14	DAY 28	DAY 0	DAY 14	DAY 28	DAY 0	DAY 14	DAY 28
Healthy	70.33 ± 3.16^{b}	70.50 ± 2.99^{b}	70.66 ± 2.99	222.83 ± 11.89^{b}	222.66 ± 11.20^{b}	222.83 ± 12.09^{b}	53.83 ± 5.32	54.00 ± 4.71	54.00 ± 4.92
Diseased	46.83 ± 1.57^{aA}	57.66 ± 2.20^{aB}	68.83 ± 2.79^{C}	164.50 ± 5.15^{a}	171.33 ± 4.16^{a}	174.16 ± 4.21^{a}	48.50 ± 5.34	56.83 ± 8.21	61.50 ± 6.71

Groups	Total Protein (gm/dL)			ALBUMIN (gm/dL)			GLOBULIN (gm/dL)		
	DAY 0	DAY 14	DAY 28	DAY 0	DAY 14	DAY 28	DAY 0	DAY 14	DAY 28
Healthy	6.06 ± 0.06^{b}	6.08 ± 0.06^{b}	6.10 ± 0.05	3.21 ± 0.06^{b}	3.25 ± 0.05^{b}	3.26 ± 0.06	2.85 ± 0.03	2.81 ± 0.03	2.83 ± 0.03
Diseased	4.46 ± 0.11^{aA}	5.01 ± 0.04^{aB}	5.95 ± 0.03^{C}	1.70 ± 0.06^{aA}	2.35 ± 0.03^{aB}	3.13 ± 0.04^{C}	2.76 ± 0.06	2.76 ± 0.05	2.81 ± 0.03

Groups	A/G Ratio			AST (µ/L)			ALT (µ/L)		
	DAY 0	DAY 14	DAY 28	DAY 0	DAY 14	DAY 28	DAY 0	DAY 14	DAY 28
Healthy	1.12 ± 0.02^{b}	1.13 ± 0.03^{b}	1.15 ± 0.03	21.49 ± 1.20^{a}	21.72 ± 1.43^{a}	21.84 ± 1.66^{a}	28.33 ± 3.72^{a}	28.43 ± 2.65^{a}	28.18 ± 3.09^{a}
Diseased	0.64 ± 0.04^{aA}	0.84 ± 0.00^{aB}	1.10 ± 0.02^{C}	30.14 ± 0.60^{b}	29.07 ± 0.49^{b}	28.66 ± 0.57^{b}	38.01 ± 1.02^{b}	36.66 ± 0.97^{b}	35.15 ± 0.83^{b}

GROUPS	BUN (mg/dL)			ALP (µ/L)			CREATININE (mg/dL)		
	DAY 0	DAY 14	DAY 28	DAY 0	DAY 14	DAY 28	DAY 0	DAY 14	DAY 28
Healthy	14.13 ± 0.43^{b}	14.66 ± 0.35^{b}	14.08 ± 0.39	98.16 ± 19.29	98.50 ± 18.99	98.66 ± 18.75	0.59 ± 0.02	0.57 ± 0.02	0.58 ± 0.03
Diseased	12.21 ± 0.41^{a}	13.16 ± 0.36^{a}	13.50 ± 0.32	93.83 ± 29.38	97.16 ± 16.71	96.66 ± 17.47	0.52 ± 0.12	0.48 ± 0.06	0.58 ± 0.06

Mean with different superscript (a, b) in columns are differing significantly in between the groups, otherwise non-significant. Mean with different superscript (A, B, C) in rows are differing significantly in between the intervals, otherwise non-significant.

Conclusion

Canine scabies is an intensely pruritic, non-seasonal, transmissible canine dermatosis, caused by infestation with the epidermal mite *Sarcoptes scabiei var canis*. It is a severely debilitating, highly contagious condition, which spreads through close contact between infested dogs or by contaminated fomites. Microscopic examination of skin scrapings of dogs with sarcoptic mange revealed presence of high numbers of eggs, developing stages and adult mites per microscopic field before start of the therapy. Sarcoptic scabiei infestation in dogs imparts alterations in various haematological and biochemical parameters. Cases were efficiently managed by using subcutaneous injections of doramectin @ 0.4 mg/kg body weight subcutaneously at weekly intervals along with standard treatment of pyoderma. Thus, doramectin could be used as a therapeutic agent for successful management of canine sarcoptic mange.

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