Plasma Zinc, Iron, Vitamin A and Hematological Parameters in Dogs with Sarcoptic Mange

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ABSTRACT

The aim of this study was to determine the concentrations of zinc, iron, vitamin A and hematological parameters in dogs with sarcoptic mange. The plasma of 24 dogs with sarcoptic mange and 6 healthy dogs were analyzed in this study. Zinc and iron levels of the plasma were measured by atomic absorption spectrophotometry. Vitamin A concentrations was measured spectrophotometrically. Plasma zinc of sarcoptic infested versus healthy dogs were found to be 1.04 ± 0.02 and 1.46 ± 0.16 µg/ml, respectively; plasma iron of sarcoptic infested versus healthy dogs was1.21 ± 0.03 and 1.66 ± 0.17 µg/ml, respectively; for vitamin A the values were 41.7 ± 1.3 and 51.25 ± 3.14 µg/dl, respectively. The hemoglobin levels for sarcoptic infested versus healthy dogs were found to be 9.49 ± 0.24 and 11.26 ± 0.50 g/dl, respectively; for hematocrit the values were 29.91 ± 0.58 and 35.13 ± 1.55 %, respectively and for total red blood cell count values were 4.82 ± 0.14 and 5.64 ± 0.47 $\times 10^6$/µl, respectively. Plasma zinc, iron and vitamin A were found to be significantly lower ($p<0.05$) in dogs with sarcoptic mange than those of healthy control dogs. Hematology results revealed significantly decreased hemoglobin, hematocrit and total red blood cell counts ($p<0.05$) in dogs with sarcoptic mange than those of healthy control dogs, however no significant change was observed in Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH) and Mean Corpuscular Hemoglobin Concentration (MCHC). Furthermore hemoglobin (r=0.63 and r=0.55), plasma zinc (r=0.58 and r=0.51) and iron (r=0.50 and r=0.23) concentrations were positively correlated with vitamin A in both sarcoptic mange infested and healthy control dogs, respectively. Our results indicate that zinc, iron, vitamin A and hemoglobin, hematocrit and total red blood cell counts were altered in dogs with sarcoptic mange.

Keywords: dogs, hematology, iron, sarcoptic mange, vitamin A, zinc.

INTRODUCTION

Sarcoptic mange is a contagious parasitic skin infection characterized by intense pruritus associated with vesiculo-papular eruptions and pinpoint crusts in combination with alopecia (1). Clinical signs of sarcoptic mange are primarily due to the host's allergic reaction to the mite, *Sarcoptes scabiei var. canis*. The predisposing factors for the development of the sarcoptic mange are not fully understood, but some of the important factors are immune status of the animal, nutritional condition and oxidative stress (2, 3, 4, 5).

Zinc is an essential micronutrient and its deficiency has been associated with several infectious and inflammatory conditions (6, 7). Zinc is an essential component of the body's antioxidant defense mechanism that plays an important role in the prevention of free radical- induced damage to tissues for maintenance of health and production (8).

Another important defense booster in living organism is vitamin A. Vitamin A has many functions, including maintenance of epithelial tissue, disease resistance and stimulatory effects on cell-mediated immunity (9). Zinc participates in the absorption, mobilization, transportation and metabolism of micronutrients, including vitamin A, mostly through its involvement in protein synthesis and cellular functions (10). Moreover, vitamin A has been found to affect zinc absorption and utilization; its deficiency may reduce absorption and lymphatic transportation of zinc by altering the synthesis of zinc dependent binding protein (10). Vitamin A has also been proposed to influence iron absorption and its deficiency produces a mild anemia (11).

The aim of the study was to evaluate the zinc and iron concentrations, hematological parameters and vitamin A status of dogs infected with sarcoptic mange and to investigate any correlation between them.

MATERIAL AND METHODS

Selection of animals

The dogs accepted to the study were recruited among the patients presented for clinical and dermatological examination to the referral hospital of the faculty. Dogs diagnosed with sarcoptic mange were included in the present study only when the presence of other dermatological conditions, diseases, or other problems was found to be absent. A total of twenty four sarcoptic mange-infested dogs (19 intact males and 5 intact females) of age ranging from 6-24 months (mean ± SE: 17.12 ± 0.77 months) with mean body weight (19.66 ± 1.30 kg) were accepted to the study. Nine were Labrador Retrievers, 5 were cross breed, 4 were Pomeranians and 3 each were Pugs and German shepherds. Another 6 dogs (four intact males and two intact females) clinically healthy, free of any ectoparasites and gastrointestinal parasites, age matched (15.45 ± 2.97 months) dogs with mean body weight (21.15 ± 2.10 kg) were used as controls. Three were Labradors Retrievers, 2 were German shepherds and 1 was a crossbreed. The control dogs included dogs which came to the clinic for routine health checks, vaccination and deworming.

The infested dogs had a history of dermatological problems for at least 2-3 weeks before presentation and were not subjected to any medication for at least 30 days prior to collection of blood samples. The feaces of the animals was microscopically examined to rule out any gastrointestinal parasites. The nutritional condition of dogs was assessed on a five-scale body condition score (BCS) (1 = very thin; 2 = underweight; 3 = ideal; 4 = overweight; and 5 = obese).

Dermatological examination

For parasitological examination glycerin was applied the edge of the skin lesion which was scraped with a sterile scalpel blade. Scraps were collected in 10% potassium hydroxide solution for microscopic examination and the parasite was identified according to their morphological characteristics (12). The dogs were clinically examined for any fleas, lice, ticks or any other ectoparasites; dogs positive for these ectoparasites were excluded from the study.

Dogs positive for *S. scabiei var. canis* mites on microscopic examination of material taken from up to three skin scrapping, free from fleas, lice and ticks and with skin lesions of alopecia, severe itching, excoriation, scabs on pinnae, neck, brisket, elbow and around root of tail were diagnosed as suffering from sarcoptic mange.

Blood Sample collection

Ten ml of blood was collected in acid washed (2% nitric acid) heparinized vials for the estimation of plasma zinc, iron and vitamin A. Ten ml of blood sample was also obtained from each healthy dog for the determination of the studied parameters and used as comparative standards. The blood sample was centrifuged at 1500 rpm for 10 min to harvest plasma. Two ml of blood was collected in EDTA for hematological assays.

Analysis of plasma zinc and iron

Two milliliters of plasma sample was analyzed for zinc and iron using Polarized Zeeman Atomic Absorption Spectrophotometer (Z-2300, Hitachi High-Technologies Corporation, Tokyo, Japan) by the method described by Kolmar *et al.* (13) with minor modifications. Briefly, 2 ml plasma sample was mixed with an equal volume of concentrated nitric acid and kept on low heat (below 90°C) for digestion on a hotplate until the volume reached 1 to 1.5ml. To this volume 2 ml of hydrogen peroxide was added and the sample was again digested until the volume reached 1 to 1.5 ml. A final volume of 10 ml was made-up by adding distilled water. The concentration of zinc and iron in digested samples were estimated by recording absorbance of digested samples in triplicates.

Vitamin A estimation

Vitamin A was estimated spectophometrically (Double Beam UV-VIS spectrophotometer, Labronics, Panchkula, Haryana, India) and the method employed was based on the Carr-Price reaction (14). Briefly 2 ml of 95% ethanol was added to 2 ml of plasma and mixed vigorously for one minute on a vortex mixer. Then 3 ml of petroleum ether was added and mixed with the help of vortex mixer for two minutes followed by centrifugation at 1500 rpm for 3 minutes. Finally 2 ml of supernatant (petroleum ether layer) was pipetted into a cuvette and absorbance was read at 450 nm against petroleum ether as a blank. A solution of β-carotene in petroleum ether at concentration 100 µg/dl to 10 µg/dl was used as standard and the concentration of the carotene was calculated from the standard curve. For the estimation of vitamin A concentration the contents in the cuvette were evaporated to which 0.1 ml of chloroform, one drop of acetic anhydride and 1ml antimony trichoride was added and read at 630 nm against the blank consisting of 0.1 ml chloroform and 1 ml antimony trichoride. The vitamin A concentration was then calculated by the formula (15).

Vitamin A (µg /dl) = OD_{630}- (OD_{450}*0.248)*361.

Hematological investigation

The total erythrocyte count (TEC) was determined using a hemocytometer (Glass agencies, Amballa cantt, Haryana, India). Hematocrit was measured by the microhematocrit method and hemoglobin concentration were determined spectrophotometerically using the cyanomethemoglobin method (Drapkins solution) (16). Mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH) and Mean corpuscular hemoglobin concentration (MCHC) were calculated.

Statistical Analysis

The data were analyzed statistically using unpaired student's t- test to determine the significance of differences between the mean values of two study groups and Pearson's correlation was used to find the correlation between the parameters. Data were expressed as mean ± standard error. Statistical significance of $p<0.05$ was considered significant.

RESULTS

All dogs were fed mainly commercial dry-food along with some home-cooked food containing mostly eggs, bread and chicken. On body condition score (BCS) assessment of dogs with sarcoptic mange, 3 dogs were found to be underweight (BCS=2), 18 were found to be optimal (BCS=3), 2 overweight (BCS=4) and 1 obese (BCS=5). All the control dogs had an optimal BCS (BCS=3). Clinical examination of dogs revealed sarcoptic mange with clinical signs of intense pruritus associated with vesiculo-papular eruptions and pinpoint crusts in combination with alopecia. Pedal pinnal reflex was positive in all cases.

No differences were detected for any of the parameters between males and females. Plasma zinc and iron levels were found to be lower in dogs with sarcoptic mange than in the healthy controls ($P\leq0.05$) however both were within the laboratory reference range for dogs. Vitamin A levels were significantly ($P\leq0.05$) lower in the sarcoptic mange dogs than in the healthy control dogs and levels were lower than the reference range for dogs established in our laboratory as shown in Table 1.

Hematological parameters revealed a significant ($P\leq0.05$) decrease in hemoglobin, hematocrit and TEC, values in dogs with sarcoptic mange than the healthy control dogs and this decrease was observed in both males and females dogs infested with sarcoptic mange. The values were however within our laboratory reference range for dogs. No significant change was observed in dogs (both male and female) in the MCV, MCH and MCHC as shown in Table 2.

Correlation analysis revealed that vitamin A is positively correlated with zinc (r=0.58 and r=0.23), iron (r=0.51 and 0.37) and hemoglobin (r=0.63 and r=0.65) in both sarcoptic mange affected healthy control dogs as shown in Table 3.

DISCUSSION

Sarcoptic mange is a contagious skin infection of dogs caused by the *Sarcoptes Scabiei var. canis.* This disease is characterized by intense pruritus associated with a vesiculo-papular eruptions and pinpoint crusts in combination with alopecia. Disorders in the proper functioning of the organism as a consequence of many diseases and stresses increase the demand for nutrients, including vitamins and mineral substances. Trace elements are required for the normal functioning of the living cells, and their concentration has been found to change as a result of infection (17, 18).

In the present study, a significantly lower level of zinc was observed in dogs with sarcoptic mange than the healthy controls. Lower levels of zinc has been reported in several

Table 1: Plasma zinc, iron, vitamin A concentrations in healthy and sarcoptic mange infested dogs

Parameters	Reference values¥	Sarcoptic mange infested	Healthy	P-value
Zinc (µg/ml)				
Male	0.71-2.37	1.05 ± 0.22 (n=19)	1.55 ± 0.21 (n=4)	
Female	0.63-2.63	1.02 ± 0.25 (n=5)	1.37 ± 0.29 (n=2)	
Combined	0.67-2.51	1.04 ± 0.02[a] (n=24)	1.46 ± 0.16[b] (n=6)	0.0483
Iron (µg/ml)				
Male	0.88-2.14	1.22 ± 0.03 (n=19)	1.75 ± 0.22 (n=4)	
Female	0.78-1.94	1.12 ± 0.08 (n=5)	1.48 ± 0.44 (n=2)	
Combined	0.83-2.04	1.21 ± 0.03[a] (n=24)	1.66 ± 0.17[b] (n=6)	0.0456
Vitamin A (µg/dl)				
Male	44.01-82.61	41.82 ± 1.67 (n=19)	52.48 ± 6.50 (n=4)	
Female	42.53-74.59	40.98 ± 1.43 (n=5)	47.86 ± 6.61 (n=2)	
Combined	43.27-78.61	41.70 ± 1.30[a] (n=24)	51.25 ± 3.14[b] (n=6)	0.0244

¥ Medicine Lab SKUAST-J (Central Laboratory for the Medicine faculty). Superscript (a & b) in a row differ significantly at 5% ($p<0.05$).

infectious diseases and inflammatory disease including dermatosis in dogs (2 ,6). During infection, interleukins are released from activated phagocytes, causing increased synthesis of metallothionein in the liver which removes zinc from the circulation (19). Extracts of *S. scabiei* have been shown to stimulate secretion of cytokines like interleukin-1α (IL-1α), interleukin-1β (IL-1 β), tumor necrosis factor-α and interferon-γ from keratinocytes, spleen, lymph node and peripheral blood mononuclear cells (20-22). These cytokines can also be generated from inflammation of the skin itself caused by physical stimulation of burrowing mites (23) and this could possibly account for one of the reasons for the decreased zinc concentration in the present study.

Sarcoptic mange has also been found to be associated with an increased oxidative stress (3, 24) where zinc is an essential components of the body's antioxidant defense (Cu, Zn SOD) that plays an important role in the prevention of free-radical-induced damage by scavenging both intra- and extracellular superoxide radicals. Thus low concentrations of zinc could also have resulted from it excessive utilization to neutralize the generation of reactive oxygen species (ROS) during sarcoptic infections. Decreased concentrations of zinc have been reported in dogs with follicular mange, buffaloes with sarcoptic mange and sheep with psoroptic mange (2, 24, 25).

Significantly low levels of vitamin A were found in dogs with sarcoptic mange and were positively correlated with zinc concentration in both sarcoptic infested and healthy control dogs (r=0.58 and 0.23, respectively). Low levels of vitamin A maybe the result of the regulatory role of zinc on vitamin A absorption (26-29) and transport (30, 31). It is also reported that changes in vitamin A concentration in plasma occur during infection and deficient animals have been found to be more susceptible to various types of infections (32). These changes are part of the defense strategies of the organism, induced by IL-1 and IL-2 (33).

To the best knowledge of the authors there are no reports of levels of vitamin A in dogs with sarcoptic mange and therefore there is a lack of data to compare with the present finding. However low levels of vitamin A has been reported in goats infested with *Linognathus africans* and *Tricostrongylidae* (34). Several other studies have found that vitamin A deficiency can alter tissue zinc concentrations (35, 36) by affecting absorption and the lymphatic transport of zinc (10). Therefore, it is not clear whether depression in plasma zinc concentrations in affected animals originated from its over-utilization to counter oxidative stress or from the over production of metallothionein or from the deficiency of vitamin A and whether vitamin A deficiency increases the susceptibility of animal to sarcoptic mange directly or indirectly by decreasing the zinc concentration. This issue requires further investigation.

There was a significant decrease in plasma iron in dogs with sarcoptic mange compared to healthy control dogs with a positive correlation with vitamin A concentration in both healthy and sarcoptic mange infested dogs (r=0.37 and r=0.51). Several studies have found a link between vitamin A and iron metabolism (37-40). Iron deficiency in the organism can originate from disorders associated with its absorption, transport, storage and cellular release. As infection is reported to block iron absorption (41), the decreased iron concentration in the present study may have been due to the parasitic infection itself (42). The removal of iron from the circulation could also have been the result of increased production of apolactoferrin removing Fe-transferrin and sequestering

Table 2: Hematological parameters in healthy and sarcoptic mange infested dogs

Parameters	Reference values¥	Sarcoptic mange infested	Healthy	P-value
Hemoglobin (g/dl)				
Male	11.03-14.18	9.53 ± 0.31 (n=19)	11.39 ± 0.57 (n=4)	
Female	10.71-13.08	9.36 ± 0.25 (n=5)	11.00 ± 0.92 (n=2)	
Combined	10.87-13.63	9.49 ± 0.24[a] (n=24)	11.26 ± 0.50[b] (n=6)	0.0137
TEC (×10⁶/µl)				
Male	5.7-8.5	4.95 ± 0.17 (n=19)	5.78 ± 0.72 (n=4)	
Female	5.3-8.2	4.78 ± 0.22 (n=5)	5.36 ± 0.63 (n=2)	
Combined	5.5-8.5	4.82 ± 0.14[a] (n=24)	5.64 ± 0.47[b] (n=6)	0.0421
PCV (%)				
Male	32.01-38.08	30.04 ± 0.62 (n=19)	35.97 ± 2.05 (n=4)	
Female	31.17-37.61	29.65 ± 1.44 (n=5)	33.45 ± 2.82 (n=2)	
Combined	31.59-37.28	29.91 ± 0.58[a] (n=24)	35.13 ± 1.55[b] (n=6)	0.0256
MCV (fl)				
Male	59.18-80.32	60.68 ± 2.24 (n=19)	62.23 ± 5.23 (n=4)	
Female	55.26-77.78	62.02 ± 1.58 (n=5)	62.24 ± 4.14 (n=2)	
Combined	57.22-79.08	62.05 ± 2.8 (n=24)	62.28 ± 4.3 (n=6)	0.896
MCH (ρg)				
Male	18.93-26.15	19.25 ± 0.92 (n=19)	19.70 ± 3.77 (n=4)	
Female	18.35-28.61	19.58 ± 0.72 (n=5)	20.52 ± 6.66 (n=2)	
Combined	18.64-27.38	19.87 ± 0.73 (n=24)	19.96 ± 2.95 (n=6)	0.731
MCHC (%)				
Male	27.85-35.23	31.72 ± 2.33 (n=19)	31.66 ± 3.89 (n=4)	
Female	25.29-34.27	31.56 ± 4.39 (n=5)	32.88 ± 9.21 (n=2)	
Combined	26.57-35.23	31.72 ± 1.08 (n=24)	32.05 ± 3.42 (n=6)	0.947

¥ Medicine Lab SKUAST-J (Central Laboratory for the Medicine faculty). Superscript (a & b) in a row differ significantly at 5% ($p<0.05$).

Table 3: Correlation and p-values between zinc, iron and hemoglobin concentrations with vitamin A in healthy and sarcoptic mange infested dogs

Parameters	Correlation(r)	P-value
Between zinc and vitamin A		
Affected dogs	0.58	≤0.05
Normal dogs	0.23	
Between iron and vitamin A		
Affected dogs	0.51	≤0.05
Normal dogs	0.37	
Between hemoglobin and vitamin A		
Affected dogs	0.63	≤0.05
Normal dogs	0.55	

iron in compartments that are nutritionally unavailable to parasites (43).

Vitamin A deficiency reduces the activity of ceruloplasmin, a copper-dependent protein with ferroxidase activity that is important in the enteric absorption of iron. However, from this statement it cannot be concluded whether the reason of the decreased iron level in infected animals is due to the use of iron by the parasite or its diversion to other parts of the body or due to the vitamin A deficiency. Future studies need be conducted to investigate the mechanisms by which iron concentrations decline under circumstances of sarcoptic infection in dogs.

Significant decreases in hemoglobin, hematocrit and total erythrocyte counts with normocytic normochromic erythrocytic indices were observed in dogs with sarcoptic mange and hemoglobin was found to be positively correlated with vitamin A concentration (r=0.55 and r=0.63, respectively) in both healthy and sarcoptic infested dogs. The decline in hemoglobin, and total erythrocytic count reported could possibly be the due to suppression of erythropoiesis due to toxic substances secreted by the parasitic mites (44). Also as sarcoptic mange is associated with increased oxidative stress the low hemoglobin, hematocrit and total erythrocytic count observed could be due to increased oxidation and damage to erythrocytes (45). Vitamin A deficiency impairs erythropoiesis and possibly results in a mild anemia and the production of deformed cells (46) which would be broken down by the macrophages of the reticuloendothelial system at an increased rate resulting into anemia (37). Thus the modest but significant decrease of vitamin A observed in the present study could also be one of the reasons for decreased total erythrocytic count, hemoglobin and hematocrit. Positive correlation between vitamin A and hemoglobin has also been reported in school children in Bangladesh (r=0.31) and in adolescent girls from Malawi (r=0.16) (47, 48).

CONCLUSIONS

In this study, we found that dogs infested with sarcoptic mange showed significantly low plasma zinc, iron and vitamin A concentrations with decreased hemoglobin, hematocrit and total erythrocytic count and these findings should be taken into consideration to improve the therapeutic approaches of sarcoptic mange. However, studies concerning the alterations in concentrations of trace elements are complicated by the fact that the trace elements are multi-functional. To this end, the monitoring of these trace elements along with vitamin A concentrations in infected animals especially with treatment opportunity may be helpful to clarify the reason for alterations in trace elements in dogs with sarcoptic mange.

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REFERENCES

1. Pin, D., Bensignor, E., Carlotti, D. N. and Cadiergues, M. C.: Localized sarcoptic mange in dogs: a retrospective study of 10 cases. J. Small Anim. Pract. 47: 611–614, 2006.
2. Dimri, U., Ranjan, R., Kumar, N., Sharma, M. C., Swarup, D., Sharma, B. and Kataria, M.: Changes in oxidative stress indices, zinc and copper concentrations in blood in canine demodicosis. Vet. Parasitol. 154: 98-102, 2008.
3. Camkerten, I., Sahin, T., Borazan, G., Gokcen, A. and Das, A.: Evaluation of blood oxidant/antioxidant balance in dogs with sarcoptic mange. Vet. Parasitol. 161: 106-109, 2009
4. De, U.K. and Dey, S.: Evaluation of organ function and oxidant/antioxidant status in goats with sarcoptic mange. Trop. Anim. Health Prod. 42:1663-1668, 2010.
5. Patel, J.S., Patel, P.R., Panchasara, H.H. and Brahamaxtri, K.G.: Epizootology of sarcoptic mange in buffalo calves. Indian Vet. J. 80:972-974, 2003.
6. Naresh, R., Dwivedi, S.K., Swarup, D. and Dey, S.: Zinc, copper, and cobalt concentrations in blood during inflammation of mammary gland in dairy cows. Asian Austral. J. Anim. Sci. 14:564-566, 2001.
7. Erksine, R.J. and. Bartlett, P.C.: Serum concentrations of copper, iron, zinc during Escherichia coli-induced mastitis. J. Dairy Sci. 76:408-413, 1993.
8. Ewans, P. and Halliwell, B.: Micronutrients: Oxidant/antioxidant status. Br. J. Nutr. 85:57-74, 2001.
9. Chew, B.P.: Vitamin A and β-carotene in host defence. J. Dairy Sci. 70:2732-2743, 1987.
10. Christian, P. and West Jr, K.P.: Interactions between zinc and vitamin A: An update. Am. J. Clin. Nutr. 68:435-441,1998.
11. Roodenburg, A. J., West, C. E., Yu, S. and Beynen, A. C.: Comparison between time-dependent changes in iron metabolism of rats as induced by marginal deficiency of either vitamin A or iron. Br. J. Nutr. 71:687-699, 1994.
12. Soulsby, E. J. L.: Helminths, arthropods and protozoa of domesticated Animals, 7th ed., Bailliere Tindall, 1982.
13. Kolmer, J. A., Spandling, E. H. and Robinson, H. W.: Applied Laboratory Techniques, Appleton Centuary Croft, New York, 1951.
14. Carr, F.H. and Price, E. A.: Colour reaction attributed to vitamin A. Biochem. J. 20:497-501, 1926.
15. Baker, H. and Frank, O.: Clinical Vitaminology, Methods and Interpretation. Interscience Publishers, London, pp. 158- 168, 1968.
16. Jain, N.C. Hematological techniques. In: Jain, N.C(ed) Schalm's veterinary hematology. 3rd edn. Lea and Febiger, Philadelphia, pp. 20-86, 1986.
17. Pasa, S., Kargin, F., Bildik, A., Seyrek, K., Ozbel, Y. and Ozensoy, S.: Serum and hair levels of zinc and other elements in dogs with visceral leishmaniasis. Biol. Trace Elem. Res. 94, 141-147, 2003.
18. Wanger, H. M., Buesher, H.U., Rollinghoff, M. and Solbach, W.: Interferon-gamma inhibits the efficacy of interleukin-1 to generate a Th2-cell biased immune response induced by *Leishmania major*. Immunobiology. 182: 292-306, 1991.
19. Swenson, G.L.K., Hallgren, R., Johansen, E. and Lindth, U.: Reduced zinc in peripheral blood cells from patients with inflammatory connective tissue disease. Inflammation. 9:189-199, 1985.
20. Arlian, L. G., Vyszenski-Moher, D. L., Rapp, C. M. and Hull, B. E.: Production of IL-1 alpha and IL-1 beta by human skin equivalents parasitized by Sarcoptes scabiei. J. Parasitol. 82:719-723, 1996.
21. Arlian, L. G., Morgan, M. S. and Neal, J. S.: Extracts of scabies mites (Sarcoptidae: *Sarcoptes scabiei*) modulate cytokine expression by human peripheral blood mononuclear cells and dendritic cells. J. Med. Entomol. 41:69-73, 2004.
22. Lalli, P. N., Morgan, M. S and Arlian, L. G.: Skewed Th1/Th2 immune response to *Sarcoptes scabiei*. J. Parasitol. 90:711-714, 2004.
23. Portugal, M., Barak, V., Ginsburg, I. and Kohen, R.: Interplay among oxidants, antioxidants, and cytokines in skin disorders: present status and future considerations. Biomed. Pharmacother. 61:412-422, 2007.
24. Dimri, U., Sharma, M. C., Swarup, D., Ranjan, R. and Kataria, M.: Alterations in hepatic lipid peroxides and antioxidant profile in Indian water buffaloes suffering from sarcoptic mange. Res. Vet. Sci. 85:101-105, 2008.
25. Dimri, U., Sharma, M, C., Yamdagni, A., Ranjan, R. and Zama, M. M.: Psoroptic mange infestation increases oxidative stress and decreases antioxidant status in sheep. Vet. Parasitol. 168: 318-322, 2010.
26. Ahn, J. and Koo, S. I.: Effects of zinc, and essential fatty acid deficiencies on the lymphatic absorption of vitamin A and secretion of phospholipids. J. Nutr. Biochem. 6:595–603, 1995.
27. Ahn, J. and Koo, S. I.: Intraduodenal phosphatidylcholine infusion restores the lymphatic absorption of vitamin A and oleic acid in zinc-deficient rats. J. Nutr. Biochem. 6:604-612, 1995.

28. Kim, E. S., Noh, S. K. and Koo, S. I.: Marginal zinc deficiency lowers the lymphatic absorption of alpha-tocopherol in rats. J. Nutr. 128:265-270, 1998.
29. Noh, S. K. and Koo, S. I.: Low zinc intake decreases the lymphatic output of retinol in rats infused intraduodenally with beta-carotene. J. Nutr. Biochem. 14:147-153, 2003.
30. Mejia, L. A.: Vitamin A–nutrient interrelationships. In Bauernfeind JC, (ed.), Nutrition basics and applied science. Academic Press Inc., New York, pp. 89-100, 1986.
31. Smith, J. E., Brown, E. D. and Smith, J. C. Jr.: The effect of zinc deficiency on the metabolism of retinol binding protein in the rat. J. Lab. Clin. Med. 84:692-697, 1974.
32. Spears, J. W.: Micronutrients and immune function in cattle. Proc. Nutr. Soc. 59:587-94, 2000.
33. Bendich, A.: Physiological role of antioxidant in the immune system. J. Dairy Sci. 76:2789-2794, 1993.
34. Tanritanir, P., Ozadal, N., Ragbetli, C., Yoruk, I., Ceylan, E. and Derger, S.: Some biochemical parameters and vitamins in the hairy goats naturally mix-infested with endo and ecto parasites (lice(*linognathus africanus)* and *Trichostrongylidae* sp.). J. Anim. Vet. Advan. 8:590-594, 2009.
35. Rahman, A. S. Kimura M. and Itokawa. Y.: Testicular atrophy, zinc concentration, and angiotensin-converting enzyme activity in the testes of vitamin A-deficient rats. Biol. Trace Elem. Res. 67:29-36, 1999.
36. Rahman, A. S., Kimura M., Yokoi, K., Tanvir, E. N. and Itokawa.,Y.: Iron, zinc, and copper levels in different tissues of clinically vitamin A-deficient rats. Biol. Trace Elem. Res. 49:75-84, 1995.
37. Roodenburg, A. J., West, C. E., Beguin, Y., Van Dijk. J.E., Van Eijk. H. G., Marx. J. J. and Beynen. A. C.: Indicators of erythrocyte formation and degradation in rats with either vitamin A or iron deficiency. J. Nutr. Biochem. 11:223–230, 2000.
38. Sijtsma, K. W., Van Den Berg, G. J., Lemmens, A. G., West, C. E. and Beynen, A. C.: Iron status in rats fed on diets containing marginal amounts of vitamin A. Br. J. Nutr.70:777-785, 1993.
39. Means, R. T, Jr.: The anemia of infection. Baillieres Best Pract. Res. Clin. Haematol. 13:151-162, 2000.
40. Crimm, P. D. and Short, D. M.: Vitamin A deficiency in the dog. Am. J. Physiol. 118:477-482, 1937
41. Beresford, C. H., Neale, R. J. and Brooks, O. G.: Iron absorption and pyrexia. Lancet. 1:255-268, 1971.
42. Spodneiwska, A., Barski, D. and Sokol, R.: Concentration of selected transition metals in layer hens non-infested and infested with *Dermanyssus gallinae.* Acta Vet. Brno. 81:307-311, 2012.
43. Marquis, J. F. and Gros, P.: Intracellular Leishmania: your iron or mine. Trends Microbiol. 15:93-95, 2007.
44. Deloach, J.R and Wright, F.C.: Ingestion of rabbit erythrocytes containing 51Cr-labeled hemoglobin by psoroptes species that originated on cattle, mountain sheep or rabbits. J. Med. Entomol. 18:345-348, 1981.
45. Al-Qudah., K. M., Gharaibeh, A. A. and Al-Shyyab, M. M.: Trace Minerals stats and antioxidant enzymes activities in calves with dermatophytosis. Biol. Trace Elem. Res. 136:40-47, 2010.
46. Roodenburg, A. J, West, C. E., Hovenier, R. and Beynen, A.C.: Supplemental vitamin A enhances the recovery from iron deficiency in rats with chronic vitamin A deficiency. Br. J. Nutr. 75:623–636, 1996.
47. Ahmed, F., Barua, S., Mohiduzzaman, M., Shaheen, N., Bhuyan, M. A., Margetts, B. M. and Jackson, A. A.: Interactions between growth and nutrient status in school-age children of urban Bangladesh. Am. J. Clin. Nutr. 58:334-338, 1993.
48. Fazio-Tirrozzo, G., Brabin, L., Brabin, B., Agbaje, O., Harper, G. and Broadhead, R.: A community based study of vitamin A and vitamin E status of adolescent girls living in the Shire Valley, Southern Malawi. Eur. J. Clin. Nutr. 52:637-642, 1998.