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The effect of supplemental antioxidants vitamin C and dimethyl sulfoxide on weight gain and survival in *T. brucei* infected and diminazene treated rats

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ABSTRACT

The effect of supplementing antioxidants, ascorbic acid (AA) and dimethyl sulfoxide (DMSO) following diminazene administration in *T. brucei* infected rats was studied by assessing weight gain, survivability, parasitemia and plasma protein levels. The first group (I) of five rats was uninfected. Four additional groups of five rats per group were infected with *T. brucei*. One of the infected groups (II) was left untreated while the remaining three groups (III, IV and V) received 3.5 $mg.kg^{-1}$ of diminazene aceturate intramuscularly. One of the three diminazene treated groups (III) received no supplements, while the remaining two received daily oral supplements of 0.5 $g.kg^{-1}$ DMSO (group IV) and 100 $mg.kg^{-1}$ AA (group V). Antioxidant supplements were initiated on the day of diminazene treatment. The daily requirements of antioxidants were dispensed in small volumes of drinking water. Fresh water was given to the animals after the drug solutions were exhausted. Overall weight gain in the groups were 208.35% (uninfected), 25.86% (infected; untreated), 208.71% (diminazene/DMSO), 155.94% (diminazene alone) and 166.75% (diminazene/AA). Weight changes were inversely related to parasitemia level in the infected, untreated group. Survival rates were 100% (uninfected); 0% (infected, untreated); 0% (diminazene alone), 25% (diminazene/DMSO) and 80% (diminazene/AA). By day 21 post treatment, parasites re-appeared in all treated groups with the diminazene group recording the highest parasitemia (2.51×10^8 compared to 1.25×10^8 and 3.98×10^7 trypanosomes/mL of blood in the diminazene/DMSO and diminazene/AA groups respectively). Plasma protein levels were significantly ($P < 0.05$) reduced in infected rats, but regained normal values following treatment. AA and DMSO supplements were superior to diminazene alone in improving weight gain and survival - two desirable outcomes in trypanosomosis.

Key words: diminazene, ascorbic acid, dimethyl sulfoxide, parasitemia, survival rate, trypanosome, rat

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Introduction

Weight loss is one of the clinical features of trypanosomosis (TAIWO, 1998). Although it has been reported that a high plane of nutrition will allow infected animals to grow at the same rate as uninfected controls (AGYEMANG et al., 1990; HOLMES et al., 2000), it has also been observed that catabolic wasting, or cachexia, breaks down body tissue, regardless of how much nutrition the patient absorbs (CHOJKIER, 2005). Tumor necrosis factor alpha (TNF alpha) and low albumin have been implicated in wasting. It has been observed that TNF alpha induces oxidative stress in skeletal muscles, generates nitric oxide, decreases myosin creatinine phosphokinase (MCK) expression and binding activities. These result in reduced production of albumin (BUCK and CHOJKIER, 1996; BUCK et al., 2001). Oxidative stress, defined as the imbalance between oxidants and antioxidants, in favor of the former, which potentially leads to damage, has been implicated in trypanosomosis. Evidence of systemic oxidative stress, manifesting as increased lipid peroxidation (EZE et al., 2008), increased production of free radicals (MESHNIK et al., 1977), and reduced systemic antioxidants (AMEH, 1984) has been presented to support the assertion that the pathogenesis of trypanosomosis involves oxidative stress, at least in part.

Trypanosome infection depletes the levels of reduced glutathione (GSH) in the blood, liver, and kidney, as well as reducing the plasma level of ascorbic acid (IGBOKWE, 1994; UMAR et al., 2000). Evidence in the recent past has revealed that fortification of body systems with natural antioxidants, such as ascorbic acid, may correct the vitiated homeostasis arising from oxidative stress (TIWARI, 1999; PIETTA, 2000). Supplementation of infected rats with vitamin C ameliorated the decreases in total protein levels in the serum, liver, and kidneys, and also prevented the depletion of endogenous antioxidants (UMAR et al., 2000). BUCK and CHOJKIER (1996) also observed that the decreased body weight, muscle wasting and skeletal muscle molecular abnormalities of cachexia were prevented by treatment of TNF alpha mice with the antioxidant D-alpha-tocopherol or the NOS inhibitor nitro-L-arginine.

In the light of current knowledge of the pathogenesis of trypanosomosis, it is conceivable that an effective treatment regimen designed to eliminate trypanosomes, reverse the pathologic processes and reduce mortality may need more than an injection of a trypanocide. Presently, data on clinical trials on the efficacy of antioxidants in trypanosomosis are limited. This study was therefore undertaken to evaluate the effects of antioxidant supplementation on animal survival and recovery of body weight in rats experimentally infected with *T. brucei* and treated with diminazene aceturate.

Materials and methods

This study was carried out on male albino rats of the Wistar strain weighing between 40 and 60 grams at the onset of the experiment. They were randomly selected and kept in five groups (I-V) of five rats per group. Each rat in each group was individually

marked. Each group was kept in a separate standard rat cage (International Biological Laboratories, Haryana, India) with wood shaving as bedding. Animals were cared for in compliance with the guidelines stipulated in the Guide for the Care and Use of Laboratory Animals (National Research Council, 2010). The institution's ethics committee approved and monitored the protocol. All animals were fed *ad libitum* with commercially formulated feed (Vital Feed, Jos, Nigeria) containing 19.00% crude protein; 8.60% fat; 5.40% crude fibre; 1.20% calcium, and 0.41% available phosphorus. Water was also given *ad libitum.* Excess feed and water were removed and replaced with fresh supplies daily.

The animals were allowed one week to acclimatize to their cages before the study began with weight recording. After five days of weight recording, the animals in groups II, III, IV, and V were infected with the Federe strain of *Trypanosoma brucei,* obtained from the Nigerian Institute for Trypanosomosis Research (NITR), Vom, Nigeria, where it had been preserved in liquid nitrogen. The parasites were maintained in the rats by serial passage after removal from the liquid nitrogen. Blood from a rat showing heavy parasitemia was diluted in normal saline to obtain trypanosome concentration of 1 x 10^5 per mL. Each animal received 0.1 mL of the diluted blood. Animals in group I were uninfected. Each animal in groups III, IV and V was treated with diminazene aceturate (3.5 mg.kg^{-1} BW) (Samorenil®; Animal Care Services Konsult, Lagos, Nigeria) on the tenth day post infection. In addition to diminazene treatment, animals in group IV received 0.5 g.kg^{-1} body weight of dimethyl sulfoxide (DMSO) dispensed in drinking water daily for the remaining period of the study. Similarly, animals in group V received 100 mg.kg^{-1} supplement of ascorbic acid (AA) daily in their drinking water. The daily DMSO and AA supplements were dispensed in small volumes of drinking water. Fresh water was given to the animals after the drug solutions were exhausted. Animals in group II were infected and untreated. All animals were weighed between 7 am and 8 am every other day from beginning to end of the study, using a digital balance (Scout Pro SPU 4001; Ohaus Corporation, New Jersey, USA).

Determination of parasitaemia and plasma protein levels. A wet smear of the tail blood of rats in the infected groups was examined using the rapid matching method of HERBERT and LUMSDEN (1976) to determine the parasitemia levels before treatment and on days 7, 14 and 21 post diminazene treatment. The plasma protein levels in all animals were determined using the biuret method, as described by TIETZ (1995).

Analysis of results. The mean body weight of a group at any time was calculated from the individual weights of the animals in the group. The rate of mass gain of a group at the end of experiment was calculated as percentage of their weights on day 1. The survival rate in each group was calculated as the percentage of surviving animals in the group after 30 days post treatment. Statistical analysis was done with Instat® software (GraphPad Inc., USA) using one-way analysis of variance (ANOVA) (for ≥ 3 means) and

two-tailed P value (for 2 means). Probability values less or equal to 0.05 ($P \leq 0.05$) were considered significant.

Results

Mass changes. All animals gained weight before infection. Weight gain by the uninfected control group was consistent and superior to the diminazene (group III) and diminazene/AA (group V) groups throughout the study period (Fig. 1). At the end of the experiment, the increase in weight in the uninfected control group was 208.35%. Similarly, the DMSO group also consistently gained weight and the group recorded 208.71% increase in weight at the end of the study. This value is comparable to that recorded in the uninfected control group. The weight gain in groups III (diminazene alone) and V (diminazene/AA) at the end of the study was 155.94% and 166.75% respectively.

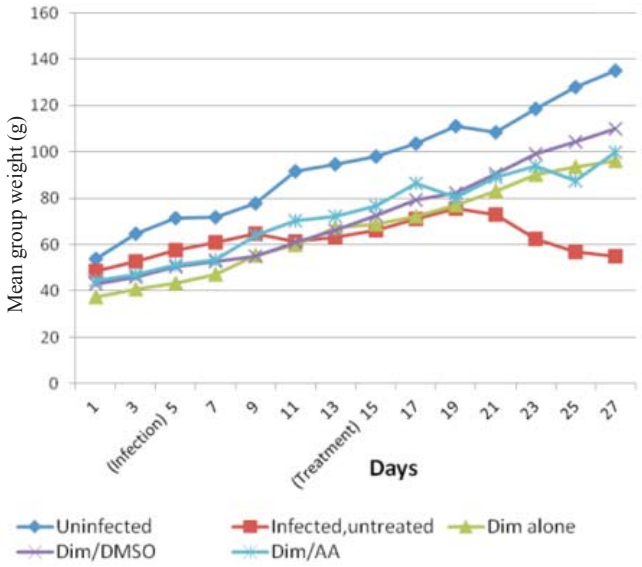


Fig. 1. Changes in the weight of rats infected with *T. brucei* and treated with a single injection of diminazene aceturate (3.5 $mg.kg^{-1}$) with and without daily supplements of ascorbic acid (AA) at 100 $mg.kg^{-1}$ or dimethyl sulfoxide (DMSO) at 0.5 g/kg^{-1}

The rats in group II (infected, untreated) gained weight consistently until day 4 post infection (4DPI) when parasites first appeared in the blood of some rats in the group. Weight gain resumed by day 7 post infection (7DPI) and declined a second and final time by 14DPI when the last surviving rat started losing weight consistently until it died on

22DPI (Fig. 1). The last record of weight of the last surviving rat was 25.86% higher than its weight on day 1 of the study.

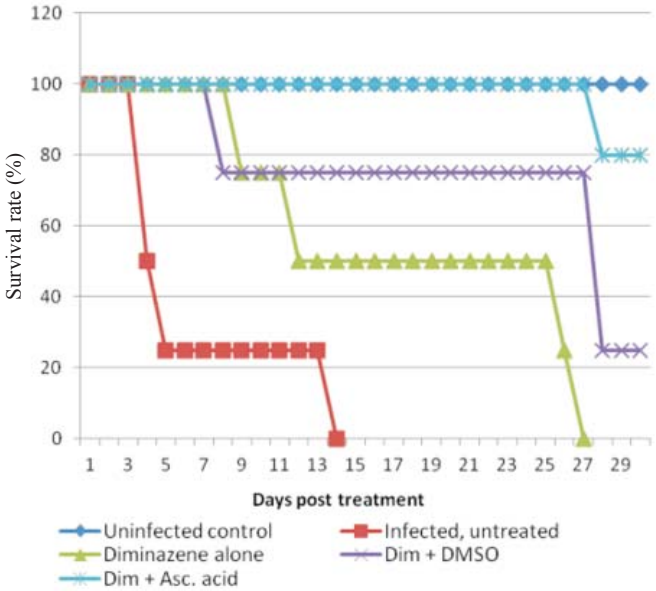


Fig. 2. The survival rate of groups of rats infected with *T. brucei* and treated with a single injection of diminazene aceturate (3.5 $mg.kg^{-1}$) with and without daily supplements of ascorbic acid (AA) at 100 $mg.kg^{-1}$ or dimethyl sulfoxide (DMSO) at 0.5 g/kg^{-1}

Survival rate. At the end of a 30 day observation period after initiation of therapy, survival rates were 100% in group I (uninfected); 0% in group II (infected, untreated); 0% in group III (infected and treated with diminazene 3.5 mg/kg alone); 25% in group IV (infected and treated with diminazene plus daily supplement with DMSO) and 80% in group V (infected and treated with diminazene plus daily supplement with ascorbic acid). The last rats in groups II and III died on days 14 and 27 respectively post treatment (Fig. 2).

Parasitemia. The prepatent period was 4-5 days following infection. By day 5 post infection (PI), all infected rats showed trypanosomes in their tail blood. Parasites were not detected in the blood of rats in groups III, IV and V on days 7 and 14 post trypanocide treatment but by day 21 post diminazene administration, parasites were detected in the blood of rats in the three groups (Fig. 3) with group III (diminazene alone) recording the highest parasitemia (2.51×10^8 trypanosomes/mL of blood) and group V (diminazene plus AA) recording the lowest (3.98×10^7 trypanosomes/mL of blood). Parasitemia in group II (diminazene plus DMSO) was 1.25×10^8 per mL of blood.

Total plasma protein. The levels of plasma protein were significantly ($P<0.05$) reduced in infected rats compared to the uninfected control (Fig. 4). Plasma protein regained its control value in all treated groups by day 7 post treatment (7DPT). There were no significant differences in the values recorded from 7DPT to 21DPT among the treated groups and also compared to the control.

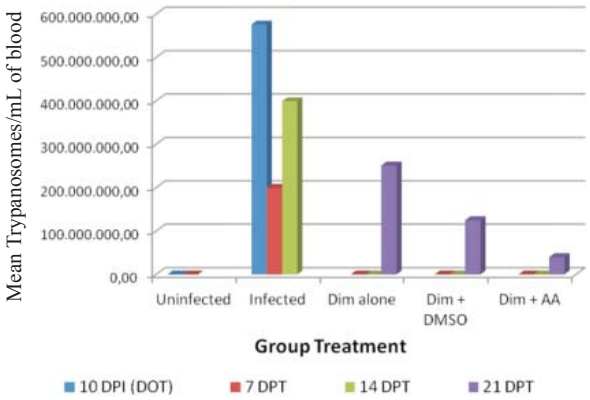
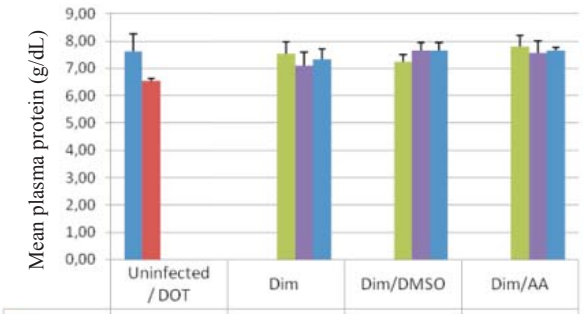


Fig. 3. Parasitemia levels in groups of rats infected with *T. brucei* and treated with a single injection of diminazene aceturate (3.5 mg.kg^{-1}) with and without daily supplements of ascorbic acid (AA) at 100 mg.kg^{-1} or dimethyl sulfoxide (DMSO) at 0.5 g/kg^{-1}



	Uninfected / DOT	Dim	Dim/DMSO	Dim/AA
Uninfected	7,63			
10 DPI	6,55			
7DPT		7,53	7,23	7,80
14DPT		7,10	7,65	7,57
21 DPT		7,32	7,65	7,66

Fig. 4. Changes in plasma protein levels in *T. brucei* infected rats

Figure 4 shows the levels in both positive and negative controls and in the groups treated with a single injection of diminazene aceturate (3.5 $mg.kg^{-1}$) with and without daily supplements of ascorbic acid (AA) at 100 $mg.kg^{-1}$ or dimethyl sulfoxide (DMSO) at 0.5 g/kg^{-1}.

Discussion

The major finding in this study is that antioxidant supplementation in combination with diminazene aceturate treatment of *T. brucei* infection led to a higher survival rate. This observation basically agrees with the results of EZE et al. (2008) who reported a higher survival rate in the group of rats treated with a diminazene/selenium combination than those groups that had selenium and vitamin E supplements alone. The positive effect of combining DMSO with conventional antiviral treatment on survival rate was reported by DAKE (1967) from his observation that all the cats died, which had an overwhelming viral infection and were treated with either DMSO alone or conventional therapy for viral infections, but the majority of the cats survived when DMSO was combined with standard antiviral treatment. The effects of ascorbic acid on survival rate has also been reported by SAHYOUN et al. (1996) from observations that subjects with plasma vitamin C levels in the middle and high quintiles had a lower overall mortality rate than those in the lowest quintile, and they concluded that high intakes and plasma levels of vitamin C may be protective against early mortality. The results of this study showed that antioxidant supplementation, in combination with diminazene treatment, improves survival rates better than diminazene treatment alone, and that ascorbic acid is more effective than DMSO in preventing mortality.

The results from this study also agree with earlier reports that trypanosome infection causes weight loss (ILEMOBADE and BALOGUN, 1981; FAGBEMI et al., 1990). In group II (infected; untreated) weight loss appeared to be inversely related to parasitemia levels. Weight gain in the group declined when parasites appeared in the blood, but weight gain resumed when parasitemia levels declined. This observation is similar to that made by NKEM et al. (2000) in *T. vivax* infection. These authors observed that serum glucose levels were inversely proportional to the level of parasitemia.

Reduced feed intake and impaired efficiency of feed conversion (ILEMOBADE and BALOGUN, 1981; HOLMES et al., 2000), fever (in association with increased heat production), increased metabolizable energy and reduction in the proportion of protein used for growth (PATHAK, 2009) and the increased synthesis of protein at the expense of muscle protein catabolism (DARGIE, 1980) have all been suggested as the cause of weight loss in trypanosome infected animals. Weight gain in the DMSO supplemented group was comparable to the uninfected group and superior to the diminazene and diminazene/ascorbic acid groups. The reasons for this are not clear, but may be due to other known

actions of DMSO. Beyond antioxidant action, DMSO possesses anti-inflammatory and analgesic activities (SANTOS and TIPPING, 1994; SANTOS et al., 2003).

The results obtained from this study, which showed reduced plasma protein in infected rats, is in consonance with those of KATUNGUKA-RWAKISHAYA et al. (1992a), who observed hypoalbuminemia in *T. congolense* infected lambs. UMAR et al. (2000) also reported significant hypoproteinemia and hypoalbuminemia as well as decreases in liver and kidney total homogenate proteins in *T. brucei* infected rats. Contrary to these findings, ABENGA and ANOSA (2005) reported increased protein levels in monkeys experimentally infected with *T. brucei gambiense*. Similarly, ORHUE et al. (2005) reported increases of total protein levels in *Trypanosoma brucei*-infected rabbits. The discrepancy between these observations may be due to differences in the species of parasites and animal hosts. It is known that the lesions caused by trypanosomes in susceptible host species vary considerably, depending on the species and strain of trypanosome, and the species and breed of host animal affected. The decrease in plasma protein level may be associated with increased urinary excretion of protein (AGU and EGBUJI, 2002) or reduced production of albumin (BUCK and CHOJKIER, 1996). The decrease in plasma albumin concentrations in trypanosome infected animals has also been attributed to uptake of albumin-bound fatty acids and lipoproteins (VICKERMAN and TETLEY, 1979) and haemodilution (KATUNGUKA-RWAKISHAYA et al., 1992b).

Relapse of infection is a well-known feature of trypanosome that has developed resistance to a trypanocide. Drug resistance by species of trypanosomes is widespread and has been reported in several studies (CHITAMBO and ARAKAWA, 1991; AFEWERK et al., 2000; ANENE and ONAH, 2001). The results of this study showed that although there were relapses in groups III, IV and V, the groups that received antioxidant supplements (IV and V) had lower parasitemia compared to group III, which received diminazene without antioxidant supplementation. The results further showed that ascorbic acid supplement was more effective than DMSO in suppressing the level of parasitemia after relapse. Only ascorbic acid (200 $mg.kg^{-1}$) and DMSO (0.5 $g.kg^{-1}$) supplementations delayed relapse beyond 21 days post treatment with diminazene at 7.0 $mg.kg^{-1}$ in an earlier observation (EGHIANRUWA et al. 2009). This discrepancy may be explained by the differences in the doses of the trypanocide and ascorbic acid used in the different studies. The doses of diminazene and AA used in this study were half those used in the earlier report. ABDULLAHI et al. (1992) observed that the dose of trypanocide used determines to a great extent the rate of reappearance of parasites after treatment.

Weight gain and survivability are two desirable outcomes that give a favorable prognosis in trypanosomosis. Ascorbic acid and DMSO supplementation performed better in these areas than diminazene treatment alone.

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References

ABDULLAHI, S. O., F. W. JENNINGS, P. H. HOLMES (1992): The rapid development of drug-resistance by *Trypanosoma evansi* in immunosuppressed mice. Acta Trop. 50, 249-257.

ABENGA, J. N., V. O. ANOSA (2005): Serum total proteins and creatinine levels in experimental Gambian trypanosomosis of vervet monkeys. Afr. J. Biotech. 4, 187-190.

AFEWERK, Y., P. H. CLAUSEN, G. ABEBE, G. TILAHUN, D. MEHLITZ (2000): Multiple-drug resistant *Trypanosoma congolense* populations in village cattle of Metekel district, north-west Ethiopia. Acta. Trop. 76, 231-238.

AGU, W. E., A. N. EGBUJI (2002): Urine albumin level in mice infected with *Trypanosoma brucei*. Vet. Arhiv. 72, 101-108.

AGYEMANG, K., R. H. DWINGER, B. N. TOURAY, P. JEANNIN, D. FOFANA, A. S. GRIEVE (1990): Effects of nutrition on degree of anaemia and liveweight changes in N'Dama cattle infected with trypanosomes. Livestock Prod. Sci. 26, 39-51.

AMEH, D. A. (1984): Depletion of reduced glutathione and the susceptibility of erythrocytes to oxidative hemolysis in rats infected with *Trypanosoma brucei gambiense*. Institute for Research in Cognitive Science (IRCS) Med. Sci. 12, 130.

ANENE, B. M., D. N. ONAH (2001): Drug resistance in pathogenic African trypanosomes: what hopes for the future? Vet. Parasitol. 96, 83-100.

BUCK, M., M. CHOJKIER (1996): Muscle wasting and differentiation induced by oxidative stress in a murine model of cachexia is prevented by inhibitors of nitric oxide synthesis and antioxidants. European Molecular Biology Organization (EMBO) J. 15, 1753-1765.

BUCK, M., L. ZHANG, L. N. A. HALASZ, T. HUNTER, M. CHOJKIER (2001): Nuclear export of phosphorylated C/EBPbeta mediates the inhibition of albumin expression by TNF-alpha. European Molecular Biology Organization (EMBO) J. 20, 6712-6723.

CHITAMBO, H., A. ARAKAWA (1991): Therapeutic effect of Berenil and Samorin in mice infected with four trypanosome populations isolated from Zambian cattle. Vet. Parasitol. 39, 43-52.

CHOJKIER, M. (2005): Inhibition of albumin synthesis in chronic diseases: molecular mechanisms. J. Clin. Gastroenterol. 39, S143-146.

DAKE, C. D. (1967): The use of DMSO in feline panleukopenia. Ann. NY. Acad. Sci. 141, 484-489.

DARGIE, J. D. (1980): Immunoglobulin metabolism in trypanosomiasis. Proceedings of the 5th International Symposium on Ruminant Physiology, MTP Press, Lancaster, pp. 349-371.

EGHIANRUWA, K. I., S. M. ANIKA, S. O. AKPAVIE (2009): Efficacy of diminazene with and without ascorbic acid supplementation in *T. brucei* infected rats. Trop. Vet. 27, 20-36.

EZE, J., B. ANENE, C. CHUKWU (2008): Determination of serum and organ malondialdehyde (MDA) concentration, a lipid peroxidation index, in *Trypanosoma brucei*-infected rats. Comp. Clin. Pathol. 17, 67-72.

FAGBEMI, B. O., E. B. OTESILE, M. O. MAKINDE, O. A. AKINBOADE (1990): The relationship between dietary energy levels and the severity of *Trypanosoma brucei* infection in growing pigs. Vet. Parasitol. 35, 29-42.

HERBERT, W. J., W. H. R. LUMSDEN (1976): Trypanosoma brucei, a rapid "matching" method for estimation of host's parasitemia. Exp. Parasitol. 40, 427-431.

HOLMES, P. H., E. KATUNGUKA-RWAKISHAYA, J. J. BENNISON, G. J. WASSINK, J. J. PARKINS (2000): Impact of nutrition on the pathophysiology of bovine trypanosomiasis. Parasitol. 120, 73-85.

IGBOKWE, I. O. (1994): Mechanisms of cellular injury in African Trypanosomiasis. Vet. Bull. 64, 611-620.

ILEMOBADE, A. A., T. F. BALOGUN (1981): Pig trypanosomiasis: effects of infection on feed intake, liveweight gain and carcass traits. Trop. Anim. Hlth. Prod. 13, 128-136.

KATUNGUKA-RWAKISHAYA E., M. MURRAY, P. H. HOLMES (1992a): The pathophysiology of ovine trypanosomiasis: Haematological and blood biochemical changes. Vet. Parasitol. 45,17-32.

KATUNGUKA-RWAKISHAYA E., M. MURRAY, P. H. HOLMES (1992b): The pathophysiology of ovine trypanosomiasis: ferrokinetic and erythrocyte survival studies. Res. Vet. Sci. 53, 80-86.

MESHNICK, S. R., K. P. CHANCE, A. CERAMI (1977): Hemolysis of bloodstream forms of *T. brucei*. Biochem. Pharmacol. 26, 19-23.

NATIONAL RESEARCH COUNCIL (2010): Guide for the Care and Use of Laboratory Animals. National Academies Press. Washington DC.

NKEM, B. K., E. O. GYANG, D. I. SAROR, A. N. ESIEVO (2000): Serum biochemical values of *Trypanosoma vivax*-infected cattle and the effects of lactose in saline infusion. Vet. Arhiv. 70, 67-74.

ORHUE, N. E. J., E. A. C. NWANZE, A. OKAFOR (2005): Serum total protein, albumin and globulin levels in *Trypanosoma brucei*-infected rabbits: Effects of orally administered *Scoparia dulcis*. Afr. J. Biotech. 4, 1152-1155.

PATHAK, A. K. (2009): Effect of Trypanosoma species on nutritional status and performance of livestock. Vet. World. 2, 435-438.

PIETTA, P. G. (2000): Flavonoids as antioxidants. J. Nat. Prod. 63, 1035-1042.

SAHYOUN, N. R., P. F. JACQUES, R. M. RUSSELL, J. MAYER (1996): Carotenoids, vitamins C and E, and mortality in an elderly population. Am. J. Epidemiol. 144, 501-511.

SANTOS L., P. G. TIPPING (1994): Attenuation of adjutant arthritis in rats by treatment with oxygen radical scavengers, Part 2. Immunol. Cell Biol. 72, 406-414.

SANTOS, N. C., J. FIGUEIRA-COELHO, J. MARTINS-SILVA, C. SALDANHA (2003): Multidisciplinary utilization of dimethyl Sulfoxide, pharmacological, cellular, and molecular aspects. Biochem. Pharmacol. 65, 1035-1041.

TAIWO, V. O. (1998): Anemia and cachexia during trypanosomiasis, putting the facts right. Trop. Vet. 16, 85-87.

TIETZ, N. W. (1995): Clinical guide to laboratory tests. 3rd ed., WB Saunders Company. Philadelphia. pp. 518-519.

TIWARI, A. K. (1999): Natural product antioxidants and their therapeutic potential in mitigating peroxidative modification of lipoproteins and atherosclerosis, recent developments. J. Med. Arom. Plant Sci. 21, 730-741.

UMAR, I. A., Z. A. TOH, F. I. IGBALAJOBI, A. GIDADO, L. B. BURATAI (2000): The role of vitamin C administration in alleviation of organ damage in rats infected with *Trypanosoma brucei*. J. Clin. Biochem. Nutri. 28, 1-7.

VICKERMAN, K. L. TETLEY (1979): Biology and ultrastructure of trypanosomes in relation to pathogenesis. In: Pathogenicity of Trypanosomes. (Losos G., A. Chouinard, Eds.). IDRC (International Development Research Centre), Ottawa. pp. 23-31.

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SAŽETAK

Učinak dodavanja antioksidanata, askorbinske kiseline (AK) i dimetil sulfoksida (DMSO), nakon primjene diminazena istražen je u štakora zaraženih parazitom *T. brucei*. Analizirana su obilježja prirasta, preživljavanja, parazitemije i razine bjelančevina u plazmi. Prva skupina (I) od pet štakora bila je nezaražena. Četiri skupine po pet štakora bile su zaražene parazitom *T. brucei*. Jedna od zaraženih skupina (II) nije bila liječena dok su preostale tri (III, IV i V) primile 3,5 $mg.kg^{-1}$ diminazen aceturata, intramuskularno. Jedna od tri liječene skupine (III) nije primila dodatak dok su preostale dvije primile oralno dnevne dodatke 0,5 $g.kg^{-1}$ DMSO (skupina IV) i 100 $mg.kg^{-1}$ AK (skupina V). S dodavanjem antioksidanata započelo se na dan liječenja diminazenom. Dnevne potrebe za antioksidantima su razdijeljene u male količine vode za piće, a svježa voda davana je životinjama nakon što je nestalo otopine lijeka. Ukupni prirast u skupinama iznosio je 208,35% (neinficirani), 25,86% (inficirani; neliječeni), 208,71% (diminazen/DMSO), 155,94% (samo diminazen) i 166,75% (diminazen/AK). Promjene u tjelesnoj masi bile su u obrnutoj vezi s razinom parazitemije u zaraženih neliječene skupine. Stopa preživljavanja bila je 100% (nezaraženi); 0% (zaraženi, neliječeni); 0% (samo diminazen), 25% (diminazen/DMSO) i 80% (diminazen/AK). Do 21 dan nakon liječenja paraziti su se ponovno pojavili u svih liječenih skupina pri čemu je u skupini liječenih diminazenom zabilježena najviša parazitemija ($2,51\times10^8$ u usporedbi s $1,25\times10^8$ i $3,98\times10^7$ tripanosoma/mL krvi kod diminazen/DMSO i diminazen/AK skupina). Razine bjelančevina plazme bile su značajno ($P<0,05$) snižene kod inficiranih štakora, ali nakon provedenoga liječenja vratile su se na normalne vrijednosti. Za dva poželjna ishoda kod tripanosomoze - prirast i preživljavanje - boljim su se pokazali AK i DMSO dodaci u odnosu na dodatak samo diminazena.

Ključne riječi: diminazen, askorbinska kiselina, dimetill sulfoksid, parazitemija, stopa preživljavanja, tripanosoma, štakor