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EFFECTS OF GRADED DOSES OF RESVERATROL ON RECTAL TEMPERATURE AND BODY WEIGHT OF *TRYPANOSOMA BRUCEI* INFECTED MALE DOGS TREATED WITH DIMINAZENE ACETURATE

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ABSTRACT

The study investigated the influence of graded doses of resveratrol on trypanosomosis induced fever and weight loss in *T. brucei* infected male dogs treated with diminazene aceturate (DA). Thirty male dogs were used for the study and were assigned into six groups (n=5). Group A was infected with *T. brucei*, not treated with (DA) and not supplemented with resveratrol. Group B was presupplemented with resveratrol (50 mg/kg) for 7 days, Infected with *T. brucei* and treated with DA (7 mg/kg). Group C was presupplemented with resveratrol (100 mg/kg) for 7 days, infected with *T. brucei* and treated with DA (7 mg/kg). Group D was presupplemented with resveratrol (200 mg/kg) for 7 days, infected with *T. brucei* and treated with DA (7 mg/kg). Groups B, C and D were postsupplemented with 50, 100 and 200 mg/kg of resveratrol for 14 days respectively. Group E was infected with *T. brucei* and treated with DA (7 mg/kg). Group F was the normal control. There were significant decreases ($p < 0.05$) in the parasitaemia level and rectal temperature of dogs supplemented with 100 mg/kg of resveratrol when compared to those supplemented with 50 mg/kg, 200 mg/kg and the infected unsupplemented group. There was a significant increase ($p < 0.05$) in weight gain of dogs supplemented with 100 mg/kg of resveratrol when compared to those supplemented with 50 mg/kg, 200 mg/kg, treated with DA alone and the infected untreated group. In conclusion, 100 mg/kg of resveratrol produced optimum activity in reducing fever and increasing body weight in DA treated *Trypanosoma* infected male dogs.

KEYWORDS: Trypanosomosis, resveratrol, diminazene aceturate, fever, body weight.

INTRODUCTION

Trypanosomosis is a protozoan disease caused by pathogenic blood parasites known as trypanosomes of the genus *Trypanosoma*. It is transmitted by tsetse flies of the genus *Glossina*. Trypanosomosis causes severe decrease in productivity, weight loss, low milk yield, poor carcass quality and decreases animal's capacity for work due to inability of infected animals to utilize available food as efficiently as healthy animals.[1,2] It has been recognized as one of the major causes of death in dogs in Nigeria.[3,4] Its common clinical manifestations are fever, weight loss, anaemia, anorexia, lethargy, weakness and dullness.[3,4]

Resveratrol is a natural polyphenol found in nuts, grapes and red wine.[5] It is known for its anti-inflammatory, antioxidant, analgesic, cardioprotective, anti-aging and neuroprotective roles.[6,7,8] Fever and anorexia induced by trypanosomosis are the major causes of weight loss in infected animals.[4] Dozens of reports have established that resveratrol prevents or slows the progression of a wide variety of illnesses.[9,10,11,12,13] Hence, the objective of the study was to determine the effects of graded doses of resveratrol on trypanosomosis induced fever and weight loss in *T. brucei* infected male dogs treated with diminazene aceturate.

MATERIALS AND METHODS

Trans-resveratrol of analytical grade was obtained from Candlewood Stars Incorporated, Danbury, USA and carboxymethylcellulose was obtained from the Department of Veterinary Physiology and Pharmacology, Faculty of Veterinary Medicine, University of Nigeria, Nsukka. Trans-resveratrol, due to its low solubility in water, was suspended in 10 g/L carboxymethylcellulose.

Trypanosoma brucei was isolated from a dog with natural infection presented to Veterinary Teaching Hospital, University of Nigeria, Nsukka and experimental animals were infected intraperitoneally at a dose of 1.5×10^6 trypanosomes per milliliter of saline diluted infected blood.

Animals

Thirty mature male dogs (Mongerels) between the ages of 6 and 7 months were used for the study. The dogs were purchased from Orba market in Enugu state, Nigeria. The dogs were housed in the Kennel unit of the Department of Veterinary Medicine, University of Nigeria, Nsukka, examined for the presence of haemoparasites, dewormed with broad spectrum anthelmintic (albendazole) and vaccinated with single doses of anti-rabies and DHLPP vaccines each. The dogs were acclimatized for two weeks before the commencement of the study. The animals were fed with home-made and commercial dog food, and water was given *ad libitum*. All protocols and handling were in accordance with the directive of Ward and Elsea and Zimmermann.[14,15]

Experimental design

Thirty male dogs were used for the study and were assigned into six groups (n=5). Group A was infected with *T. brucei*, not treated with (DA) and not supplemented with resveratrol. Group B was presupplemented with resveratrol (50 mg/kg) for 7 days, Infected with *T. brucei*, treated with DA (7 mg/kg) on day 23 and post supplemented with resveratrol (50 mg/kg) for 14 days. Group C was presupplemented with resveratrol (100 mg/kg) for 7 days, infected with *T. brucei*, treated with DA (7 mg/kg) on day 23 and post supplemented with resveratrol (100 mg/kg) for 14 days. Group D was presupplemented with resveratrol (200 mg/kg) for 7 days, infected with *T. brucei*, treated with DA (7 mg/kg) on day 23 and post supplemented with resveratrol (200 mg/kg) for 14 days. Group E was infected with *T. brucei* and treated with DA (7 mg/kg) on day 23. Group F was the normal control.

Determination of parameters

Parasitaemia was monitored using the wet mount method daily after infection, daily after establishment, daily after treatment for clearance and weekly post clearance up to 10 weeks for relapse. The numbers of infective trypanosomes were determined using the rapid matching method.[16] Rectal temperature was determined using a digital clinical thermometer and body weight was determined with a weighing balance.

STATISTICAL ANALYSIS

The data obtained from the study were analyzed using one way analysis of variance (ANOVA). Means were compared using Duncan's multiple range tests. Significant level was accepted at $p<0.05$.

RESULTS

Effects of graded doses of resveratrol on parasitaemia levels of *T. brucei* infected male dogs

Parasitaemia was established in groups A, B, C, D and E on days 5, 7, 7, 5 and 5 respectively. There was a significant decrease ($p < 0.05$) in the parasitaemia level of dogs supplemented with 100 mg/kg of resveratrol when compared to those supplemented with 50 mg/kg, 200 mg/kg and the infected unsupplemented groups. There was parasite clearance 24 hours post treatment in all the groups which did not relapse throughout the study period (Figure 1).

Effects of graded doses of resveratrol on rectal temperature of *T. brucei* infected male dogs

There was a significant decrease ($p < 0.05$) in rectal temperature of dogs supplemented with 100 mg/kg of resveratrol when compared to those supplemented with 50 mg/kg, 200 mg/kg and the infected unsupplemented groups (Figure 2).

Effects of graded doses of resveratrol on body weights of *T. brucei* infected male dogs

There was a significant increase ($p < 0.05$) in body weight of dogs supplemented with 100 mg/kg of resveratrol when compared to those supplemented with 50 mg/kg, 200 mg/kg and the infected unsupplemented groups (Figure 3).

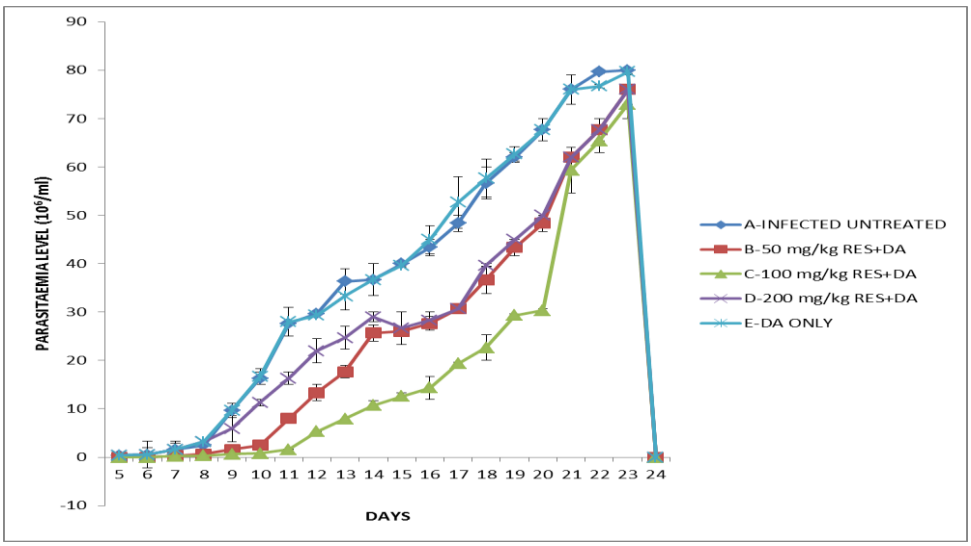

Figure 1: Effects of graded doses of resveratrol on parasitaemia levels of *T. brucei* infected male dogs.

Key: RES – resveratrol, DA – diminazene aceturate

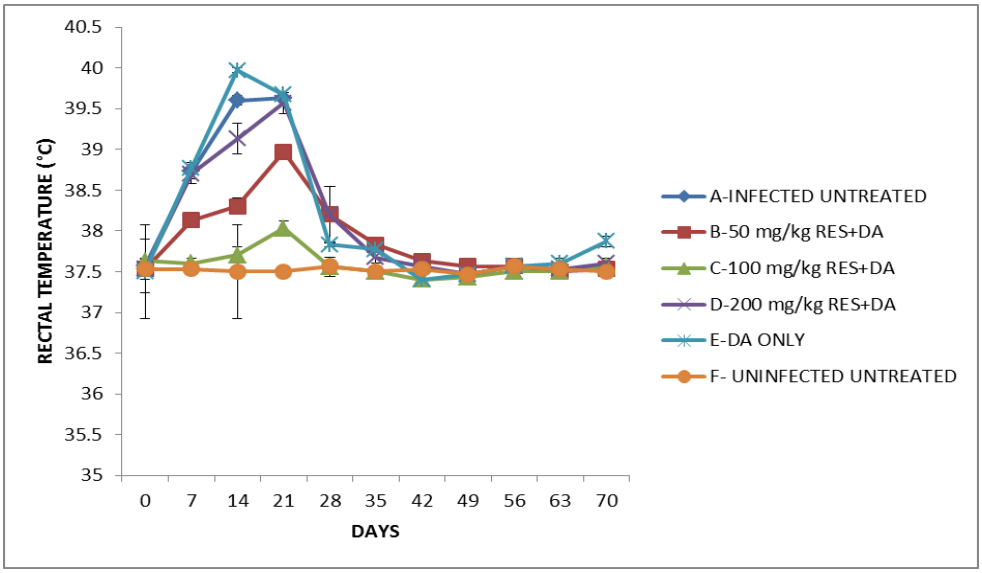

Figure 2: Effects of graded doses of resveratrol on rectal temperature of *T. brucei* infected male dogs.
Key: RES – resveratrol, DA – diminazene aceturate

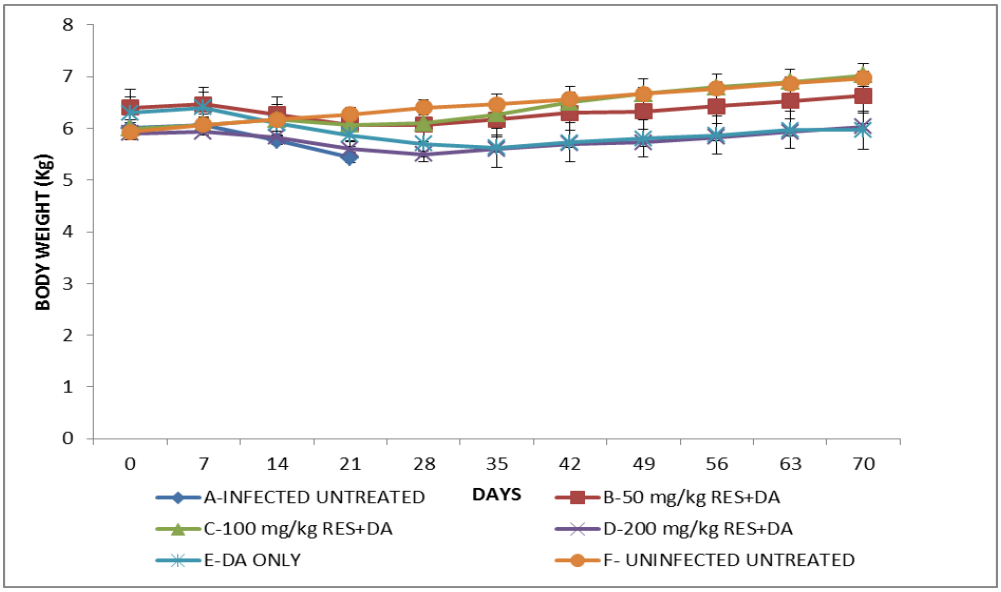

Figure 3: Effects of graded doses of resveratrol on body weights of *T. brucei* infected male dogs.
Key: RES – resveratrol, DA – diminazene aceturate

DISCUSSION

Parasitaemia was established in groups A, B, C, D and E on days 5, 7, 7, 5 and 5 respectively. Establishment of parasitaemia was delayed till day 7 in groups B and C that were supplemented with 50 mg/kg and 100 mg/kg respectively. This agrees with reports that resveratrol prevents or slows the progression of illnesses.[9,10,11,12,13]. The significant decrease ($p < 0.05$) in the parasitaemia level of dogs supplemented with 100 mg/kg of resveratrol when compared to those supplemented with 50 mg/kg, 200 mg/kg and the infected unsupplemented groups suggests that resveratrol at the dose of 100 mg/kg has optimum protective effect against early establishment of trypanosomosis.

The significant increase in the rectal temperature and significant decrease in body weight of the untreated *T. brucei* infected dogs agreed with earlier reports.[2,17,18] The significant increase in the rectal temperature and significant decrease in body weight of the untreated *T. brucei* infected dogs may be due to fever and anorexia respectively associated with trypanomosis. The significant decrease ($p < 0.05$) in rectal temperature of dogs supplemented with 100 mg/kg of resveratrol when compared to those supplemented with 50 mg/kg, 200 mg/kg and the infected unsupplemented groups may be due to optimum protection of 100 mg/kg of resveratrol against fever associated with trypanosomosis. The 200 mg/kg of resveratrol increased rectal temperature significantly ($p < 0.05$) when compared to 100 mg/kg. This may be due to overdose as high-dose of resveratrol supplementation has been reported to cause hyperthermia, reduced blood cells and decreased blood pressure.[13,19]

The significant increase ($p < 0.05$) in body weight of dogs supplemented with 100 mg/kg of resveratrol when compared to those supplemented with 50 mg/kg, 200 mg/kg and the infected unsupplemented groups may be due to optimum prevention of anorexia associated with trypanosomosis by 100 mg/kg of resveratrol. The 200 mg/kg of resveratrol may have suppressed appetite in the supplemented group, hence, the observed significant decrease in body weight of the group. One theory about why appetite suppression occurs from taking excess resveratrol is that the antioxidants in this nutrient excessively activate receptors in the upper intestinal tract to signal the brain that the appetite has been satisfied.[20] Excess intake of resveratrol also decreases cortisol, a hormone that increases appetite, and also induces the release of the hormone leptin, which suppresses appetite, leading to decrease in body weight.[21]

In conclusion, the result obtained from this investigation implies that resveratrol supplementation at the dose of 100 mg/kg in combination with DA cleared parasitaemia, reduced fever and increased body weight faster than DA alone.

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