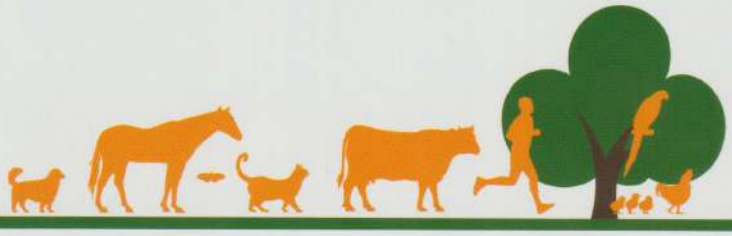
INTERNATIONAL CONGRESS ON ONE HEALTH AND AAVS-MyOHUN-WPSA (MALAYSIA)-SEAOHUN MEETINGS 2019

PROCEEDINGS

"ENHANCING GLOBAL HEALTH & WEALTH"

24-28 JUNE 2019 - MARRIOTT HOTEL, PUTRAJAYA, MALAYSIA



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TRICHOSANTHES CUCUMERINA AS A PROMISING NON-TOXIC ANTIMALARIAL AGENT AGAINST *PLASMODIUM BERGHEI* NK65 IN ANIMAL MODEL

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ABSTRACT

As the most threatening human parasitic disease, the malarial etiological agents were reported to be resistant against nearly all current antimalarial drugs. This study demonstrated how the manipulation of natural planted vegetable, *Trichosanthes cucumerina* promisingly can solve a manifestation of this disease in animal model. The four days suppression test (4DST) in *Plasmodium berghei* NK65-infected male mice (25-30 g, 6-8 weeks old) showed that 82.5 % of the inhibition rate by *T. cucumerina*-dH_2O extract at 10 mg/kg body weight (bw) and 50 % of the treated mice had survived for more than 9 months post-infection. Besides, there was a positive relationship between the mice survival and the ability to inhibit the parasites growth. The results for biochemical tests were significantly situated in the normal ranged and histologically, no abnormalities found on the selected vital organs. This study evidenced that *T. cucumerina* has a promising antimalarial activity and could be manipulated for the welfare of both animal and human, as well as for environmental sustainability.

Keywords: *Trichosanthes cucumerina*, *Plasmodium berghei NK65*, antimalarial, toxicity

INTRODUCTION

Until today, malaria is considered as neglected disease in the tropical regions in which hundreds of millions of population are at risk (Kilama & Ntoumi, 2009). Antimalarial treatment is dependent on chemical synthetic drugs which are facing development of resistance. *Trichosanthes cucumerina* or known as snake gourd is one of the crops that widely planted especially in India and Southeast Asian (Hasanuzzaman *et al.* 2004) and has many promising medicinal values (Sandhya *et al.* 2010). By far, there are very limited studies documented on the antiparasitic effects of *T. cucumerina*, particularly against malarial parasites. This study was aim to evaluate the *in-vivo* antimalarial activities of freeze-drying undergoes aqueous *T. cucumerina* extract against *Plasmodium berghei* NK65. Besides, the toxicity assessment of vital organs and enzymes activity of the mice was also investigated.

MATERIALS AND METHODS

Aqueous extract of T. cucumerina

T. cucumerina was cut into small 2-3 cm and washed with dH_2O. The remaining was blended with 2000 mL dH_2O and allowed to stand overnight at 28°C before it was being filtered and repeated for three times. Finally, 250 g of freeze-dried aqueous extract in powder form was diluted into sdH_2O to achieve its targeted dosage and concentration of 0.2 mL of 5, 10, 50, 100 and 200 mg/kg bw.

Experimental animal

With ethical approval code IIUM/IACUC Approval/2016(8)(21), every male mice group (20 – 25 g bw, 6 – 8 weeks old, n = 6/group) have been placed in stainless steel cages at room temperature and treated *ad-libitum* daily meal at 12-12 hours both with and without light periods.

Parasite inoculum

Every experimental mouse were intraperitoneally administered with the parasite inoculum consisted of 1.0×10^7 *P. berghei* per 0.1 mL Alsever's solution and the time of infection is referred as day zero (D0).

Parameters for in-vivo toxicity assessment

Blood samples (0.8–1.0 mL) of the sacrificed mice were extracted from both acute and sub-acute toxicity exposure of the mice groups before it has been undergone for biochemistry tests and compared with the data from Research Animal Resources, University of Minnesota. Two vital organs, kidney and liver from these anesthetised mice were also extracted for organ histopathology studies.

Statistical analysis

Using the Shapiro-Wilk test, all the results for antimalarial screening and biochemical toxicity assessment were expressed as the mean ± standard deviation (sd). Statistical significance was met when *P* value was equal to or less than 0.05 ($P \leq 0.05$).

RESULTS AND DISCUSSION

With less than 2.0%, this is the lowest value for parasitemia density between the G10 mice (treated with 10 mg/kg bw of *T. cucumerina* aqueous extract) and the other four groups. Besides, the inhibition rate value for G10 and G50 groups was the only values where antimalarial activities could be best evaluated (≥70%). This was in parallel with the statements that the lower the parasitemia density, the higher the inhibition percentage (Abdulelah and Zainal-Abidin, 2007). Besides, the mice of G10 were recorded as the most prolonged survival period (≥285 days) among all experimental groups. there were a significant difference ($P<0.05$, $n=6$) for parasitemia density (%), inhibition period (%) and mice survival period (day), between the G10 mice and the rest of the groups except positive control mice which treated with single dose of 0.1 mL of 15 mg/kg bw of primaquine. The results for all biochemical toxicity tests were within the normal range. Microscopically, all selected H&E stained kidney and liver tissues from the mice showed no abnormalities and injuries. Enzyme levels are often associated with infectious diseases, immune-mediated disease and some types of cancer (Ganheim *et al.*, 2007) and become the most reliable indicator for liver damage and malfunction (Craig *et al.*, 2012).

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