SUMMARY

THE TRYPNOCIDE ASSAY OF DIMINAZENE ACETURATE

The effective regimented dose design and toxicity investigated of consequence drug multiple administration on trypanosomiasis Etawa breed goats

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Cases of trypanosomiasis in Indonesia animal husbandries has been a problem for the Indonesian livestock society since 1897. An eradication effort using chemotherapeutics (namely suramin) has been used as a barrier against the trypanocide agent. Diminazene aceturate is also used as an alternative drug, and in the future antitrypanosomes may be used. The problem remains how to find a regimented dose for the various isolated cases within Indonesia. Much research has to be done to find a dose that is powerfull enough to be effective yet safe for use in animals.

The research to find this, ideal, dose will consist of three stages : (a) A pre clinical stage, (b) dose design stage and (c) clinical trials. It is intended to use the Etawa breed of goats for this research and Trypanosoma evansi Bangkalan Isolates as the parasitic agent. Stage one, pre clinic will be sub-divided into five stages they are : (a.1) In vitro trypanocyde assay, (a.2) antigenic assay, (a.3) optimation-validation high performance liquid chromatography (HPLC), (a.4) a kinetic study of the diminazene aceturat, (a.5) dose vs. respon on trypanocide. The regimented dose design stage will work by (b) superimposing concept with multiple drug administrated. The clinical trials stage will be evaluated by (c.1) trypanocide assay, and (c.2) toxicity assay. The length of time the drug concentration exceeds the therapeutic concentration level (c.3)

measured in clinical trials stage. In the research stage, the trypanocyde in vitro concentration of diminazene aceturate obtained 8.48 μg/ml and the cumulative parasitic infection dose obtained 23.10^5 Trip/ml. The HPLC analysis using the isocratic method (λ 370 nm) determined the recovery at 83.874 – 88. 178 % (KV 3.08-4.85 %). The limit of detection and limit of quantification were 8.10^{-3} μg/ml and 24.10^{-3} μg/ml. The maximum concentration in infected and healthy goats was 21.4 ± 10.3 μg/ml and 40.8 ± 24.9 μg/ml respectively. The average parameter of T½β was obtained thus 83.5 ± 26.97 Jam^{-1}. The pharmacogenetic profile of T½β on infected and healthy goats was bimodal models. The two modes being at 82,67 jam^{-1} and 131 jam^{-1}. The result study of dose respon suggested that 5 mg/kg bw would have an adequate effect against trypanocyde. This regimented dose design concluded that for effect an initial dose of 10.44 mg/kg bw, be follow by, four additional doses at a concentration of 7 mg/kg bw, administered every 31 minutes. The result clinical trials showed a marked effect against trypanocide with no toxic side effect when applied ($p<0.05$). The dose used was effective in all trypanocyde test. The length of time the drug concentration exceeds the therapeutic concentration level obtained at ≥ 24 hours ($p>0.05$).

The results of the trials proved that using the doses mentioned in the previous paragraphs trypanocide was erradicated in all the clinical subject. Research recommendations were that the new regimen may be used as an alternative to present methods when treating trypanosome.

ABSTRACT

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The effective regimented dose design and toxicity investigated of consequence multiple drug administration on trypanosomiasis Etawa breed goats

Cases of trypanosomiasis in Indonesian animal husbandries has been a problem for the Indonesian livestock society since 1897. The major problem in controlling trypanosomiasis was in the use of available medicines. This problem was exascerbated by the fact that suramin the main medicine used was not produced again except for research purposes. The Indonesian Government recommended other trypanocide agents (isometamidium chloride and diminazene aceturate) wich were readily available within Indonesia for the treatment of trypanosomiasis. However research had shown that isometamidium chloride was particularly ineffective unless used in exceptionally high doses. Because of these ongoing problems it was decided that more research was needed both into the disease and the dose level (of diminazene aceturate) to obtain a new dosage regimen with trypanocide activities and prevent toxic side effects.

The experimental research used three design they were : pre, true and quasi experimental. The parasites used in the research were of the Trypanosoma evansi Bangkalan Isolates. The subjects of the research were Etawa breed goats sourced from the Surabaya area. To determine the concentration of diminazene aceturate, goat plasma was screened using reverse-phase high performance liquid chromatography, with ion pairing. To examine the parasites within the blood samples were examined using biological assay and card aglutination base on common surface antigen. To discover the toxic effect of medicines used in the research, a screen of ante mortem toxic symphtome was used continuously with liver and renal histopathology techniques.

The research indicated that the new dosage regimen should be used as follows ; (a) loading dose 10.44 mg/kg body weight, (b) maintenance dose 7 mg/kg body weight. (c) After the initial dose of 10,44 mg/kg bw fourth additional maintenance dose should be administered at 31 minute intervals. This formula will work effectivly against Trypanosoma evansi Bangkalan Isolates and safety for using ($P<0.05$). The length of time the drug concentration exceeds the therapeutic concentration level obtained at $\geq$ 24 hours ($p>0.05$).

The results of the test confirm that the new dosage regimen may be used as an alternative model when giving diminazen aceturate as a remedy against ruminan trypanosomiasis.

Key Words : *Trypanosoma evansi, Diminazene aceturate Superimpose, Dosage Regimen, Toxicity*