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AFRICAN TRYPANOSOMIASIS: A REVIEW ON CHEMOTHERAPY

Nileshkumar Pagrut[1], Dr. Subha Ganguly[2]* and Piyusha Bhainsare[3]

[1]Associate Professor, Department of Veterinary Pathology, [2]Associate Professor, Department of Veterinary Microbiology, Arawali Veterinary College (Affiliated to Rajasthan University of Veterinary and Animal Sciences, Bikaner), N.H. – 52 Jaipur Road, V.P.O. Bajor, Dist. Sikar (Rajasthan), India.
[3]Assistant Professor, Department of Veterinary Medicine, Mahatma Jyotiba Fule College of Veterinary and Animal Science (Affiliated to Rajasthan University of Veterinary and Animal Sciences, Bikaner), N.H. – 52 Jaipur Road, Dist. Chomu (Rajasthan), India.

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***Corresponding Author**
Dr. Subha Ganguly
Associate Professor, Department of Veterinary Microbiology, Arawali Veterinary College (Affiliated to Rajasthan University of Veterinary and Animal Sciences, Bikaner), N.H. – 52 Jaipur Road, V.P.O. Bajor, Dist. Sikar (Rajasthan), India.
ganguly38@gmail.com,

ABSTRACT

The increased drug development costs, the generally small drug budgets of developing countries and widespread evolution of drug resistance are primary causes. The most striking thing about that no new effective drugs for trypanosomiasis, human or animal.

KEYWORDS: Chemotherapy, Drugs, Trypanosomiasis.

INTRODUCTION

There is restricted commercial production of suramin, tryparsamide and melarsen. pentamidine, effective only in early infections, and melarsoprol, requiring hospital admission because of toxicity, are not satisfactory treatment substitutes. Pharmacological investigations with Berenil[1,2] have shown that it is capable of prolonged tissue retention. Berenil is hydrolysed extensively in the stomach, but the effects of oral dosage on prophylaxis appear to be variable.

Development of Newer Drugs for Chemotherapy

A Berenil analogue, 6-amidino-2-(4-amidinophenyl)-indole, (1021198: DAPI) was found to be active on *Tryoanosoma congolense*- infected zebu cattle[3] and had activity equivalent to Berenil in experimental infections.[4] Trials of the adenine nucleoside, Cordycepin, in *tse tse* fly induced *T. vivax* infections[5] revealed therapeutic but not curative activity.

Drug Resistance

T. vivax and *T. congolense* strains show various degrees of resistance to Berenil, Ethidium, Antrycide and Samorin. Retained resistance after tsetse transmission for periods of up to 16 months.[6]

Combination Chemotherapy

Combination chemotherapy in the dearth of new drugs forces consideration of the possibilities of combined treatment. Development of hypersensitivity to one trypanocidal drug in a strain made resistant to another, appears to be related to synergistic activity.[7]

Mode of Action of Different Drugs

Diamidines and Ethidium cause different kinds of kinetoplast DNA condensation in *T. cruzi in vitro*[8-10] and in *T. rhodesiense in vitro.*[11] These effects may reflect a difference in mode of binding, which is intercalative for Ethidium and external for diamidines.[12] Berenil appears to bind to *T. cruzi* kinetoplast circular DNA at four equidistant sites which also bind RNA polymerase.[13] Another important cytotoxic property of diamidines, the ability to precipitate nucleoside phosphates and nucleotide coenzymes has been emphasized.[14] *T. vivax- 7' congolense* (haematic) and *T. brucei* (humoral) trypanosomes are differentially distributd among the mammalian populations.[15-18]

CONCLUSION

Out of Antrycide, Ethidium and Berenil, only Berenil shows considerable *in vitro* tissue retention and hence is more active in vivo against *T. brucei* tissue forms.

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