STUDY OF STATE OF RESISTANCE TO REINFECTION WITH *Schistosoma mansoni* AFTER EITHER SPECIFIC CHEMOTHERAPY OR IMMUNOADJUVANTS

BY

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B.Sc. in ZOOLOGY

THEODOR BILHARZ RESEARCH INSTITUTE

Thesis

SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS.

FOR THE

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IN

ENVIRONMENTAL SCIENCES

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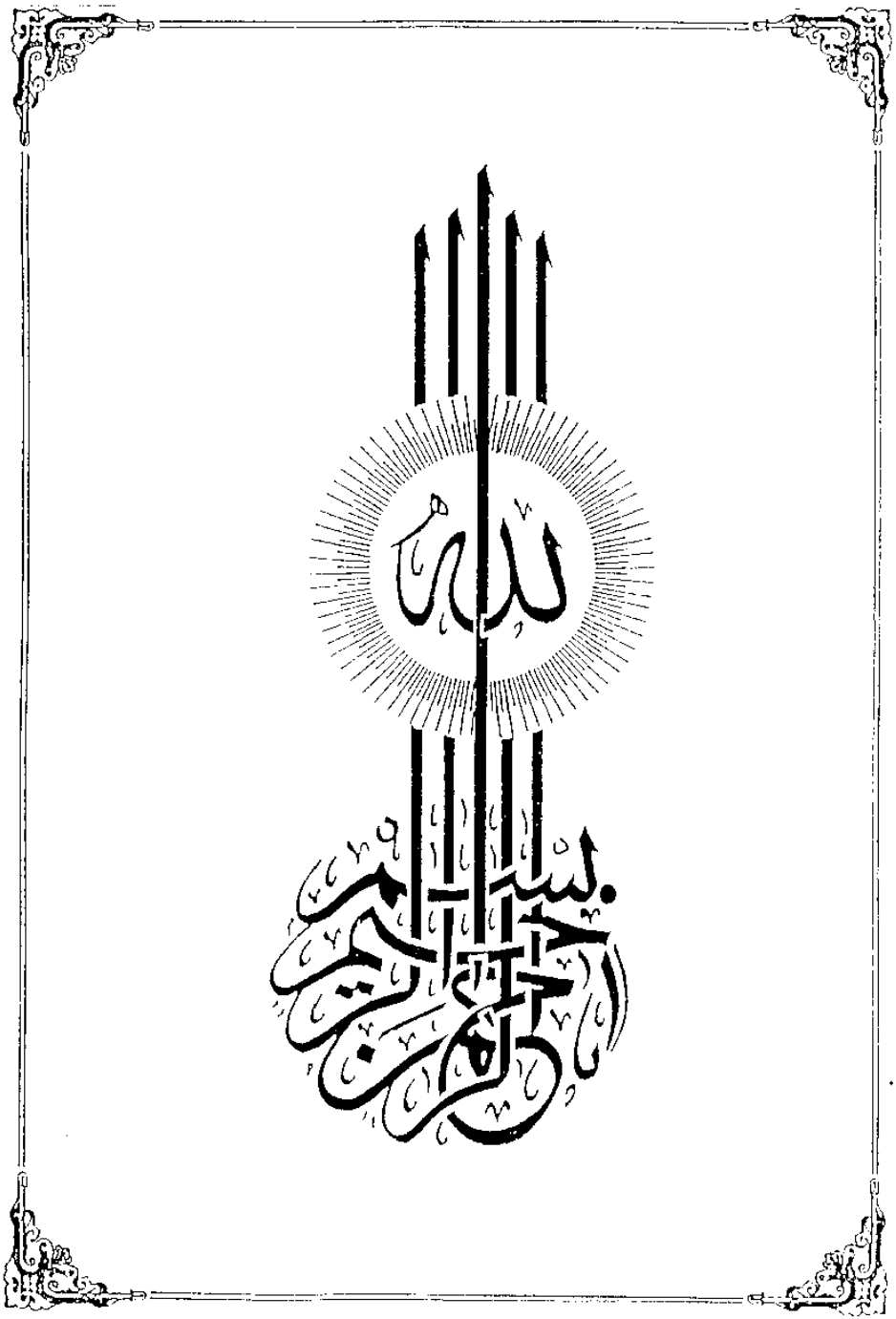

بسم الله الرحمن الرحيم

وما أوتيتم من العلم إلا قليلا

صدق الله العظيم

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INTRODUCTION

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Human schistosomiasis is a major health problem in the subtropical and tropical countries of the world, affecting more than 200 million people, Mahmoud **and Robinson,. (1977).**

The world health organization estimates that about 600 million people are at risk of developing this disease, out of whom about one half may actively suffer from the disease and require treatment. It is further estimated that, about one third of those requiring treatment, about 100 millions, are in Africa (Magugu, 1980).

Schistosomiasis has been long considered as the major health problem in Egypt due to high prevalence and morbidity of the disease among the Egyptians especially the rural population. The disease and its complications affect production potentials and thereby reduce the national income.

The majority of people infected with *Schistosoma mansoni* and living in endemic areas, have a low worm burden as judged by fecal egg counts (Kloetzel, 1973 and Cook *et*

al., 1974) and by counting of worms after postmortem perfusion of the porto-mesentric system (Cheever, 1968). Why they do not acquire heavier infections although being constantly exposed to infecting waters, is not completely known.Up to the present no immunolgical indicators are available to assess resistance to reinfection.

Immunity in the presence of active infection was first described in rhesus monkeys, where adult *S. mansoni* derived from a primary infection persisted long after resistance to a challenge infection had developed (Smithers and Terry, 1965).The phenomenon was called "concomitant immunity".The concept of concomitant immunity in schistosomiasis is based on the finding that an established population of adult worms from primary infection persists long after resistance has developed to a challenge infection (Smithers and Terry, 1969).

The chemotherapy of schistosomiasis, and the elimination of the adult worms from an infected individual will undoubtedly lead to changes of the specific immune reactivities of that host. If concomitant immunity disappears, the possibility that the next infection would be a heavy one exists.Changes in the state of resistance after

worm eradication by specific chemotherapy has been the subject of intensive study.

Experimental data in the literature are controversial on this subject, since both susceptibility (Cheever et al.,1965; Doenhoff et al., 1980 and Andrade & DeBrito, 1982) and resistance to reinfection (Warren, 1977) have been reported after chemotherapy of *S. mansoni* infection. Using praziquantel to cure *S. mansoni* infected animals, a diminished state of resistance was reported when those animals were challenged by *S. mansoni* cercariae (Botros *et al.*, 1989 and Hassan *et al.*, 1990). Restoration of this compromised state of resistance was reported by the above authors when using levamisole (Ketrax), a broad spectrum anthelminthic with known immunostimulatory property. Although restoration of that immunity was reported by the previous authors after praziquantel & Ketrax the reported defect to the hepatocytes "toxicity" after the use of this drug, is a limiting factor. In the present work, a new immunomodulatory drug with minimal side effects, is going to be tested after a compromised state of immune response has been induced by specific chemotherapy.

Analysis of the effector mechanisms involved in defense against schistosome infection has shown that both specific and non specific immunologic mechanisms are operating. The immunologic mechanism directed against the egg has been incriminated by some authors to be acting non specifically in the cytocidal action against schistosomiasis larvae (Dean *et al.*,1978a, Bickle *et al.*, 1980 and Colley & Freeman 1983). Recently, more evidence has developed which demonstrates that at least a major part of resistance is immunologically based (James & Cheever, 1985).

AIM OF THE WORK

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The aim of this work is to determine four important criteria:

1- To what extent the maintenance of a state of resistance is dependent on the persistence of a primary infection in *S. mansoni* infected experimental mice.

2- The effect of specific chemotherapy and combination of an antibilharzial drug (Praziquantel) with a safe immunostimulant drug (Synthetic Adamantylamide Dipeptide) on the degree of resistance after cure.

3- The possible involvement of humoral immune responses in maintenance of a state of resistance to reinfection as determined by the percent lymphocytes forming erythrocyte antibody complement (EAC) rosettes.

4- Possible involvement of the cellular immune response was assessed using hepatic granuloma measurements and enumeration of T-cell subsets in the hepatic granuloma.