# CERTAIN STUDIES ON AMINO ACIDS REQUIREMENTS AND METABOLISM IN EXPERIMENTAL SCHISTOSOMIASIS

BY

MOHAMED ALY SABER

B.Sc. Agric.
Faculty of Agriculture
Ain Shams University.
(1965)

Diploma of Microbiology
Faculty of Science
Cairo University.
(1966)

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Faculty of Agriculture
Ain Shams University.
(1970)

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This disseration has not previously been subuitted for a degree at this or at any other university.

The referances in the text will show the extent to which I have availed myself of the work of the other authors.

Signed

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This Thesis for the M.Sc.

Degree has been Approved

by:

Committee in Charge

Date / /

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# I N T R O D U C T I O N

# INTRODUCTION

In U.A.R. bilharziasis is highly endemic and constitutes not only a major public health hazard, but also a great socio-economic problem. The disease is not directly a killing one, but causes gradual deterioration of health and man power , retardation of intellectual development and finally reduction in the total economic production. Our health authoroties having realized this fact, started combating this disease many years ago.

Three species of schistosomes are responsible for bilharziasis in man; Schistosoma mansoni; Schistosoma haematobium; and Schistosoma japonicum. The latter is restricted to the Far East and not present in U.A.R.. In this respect most of the experimental studies have been carried on Schistosoma mansoni, as this species is more suitable for experimental chemotherapy.

The control programme in general based on the following lines:-

1) Mass chemotherapy.
2) Environmental sanitation and health education.
3) Snail control.

Extensive research projects in the field of mass chemotherapy are still needed searching for more tolerable, easily administrable as well as effective and less costly drugs. It is clear that the first approach towards the solution of this problem is to learn more fundamental facts concerning the exact metabolic pathways used by the adult schistosomes. Also, the importance of determining the nutritional requirements and the absorptive mechanism of these parasites have to be emphasized.

For many years, biochemical studies in experimental schistosomiasis have been directed towards the invistigation of the changes in certain metabolic patterns and serum enzymes of the host. In comparison, much less work has been done on the metabolic activites of schistosomes. Reliable information on the metabolism of these parasites is still very limited and much remain unknown of their carbohydrate, fat, and protein metabolism as well as of the active transport system across cuticle and gut. Progress in these fields will ultimatelly furnish knowledge that would lead to a more rational and more effective therapy.

The current trend of research is emphasizing the significance of learning more fundamental facts concerning

the metabolic pathways used by schistosomes and of determining their nutritional requirements. Also, the importance of enzymatic studies is indicated from the well known fact that much of our knowledge about the pathways of metabolism in higher animals have come from the in-vitro studies of enzymes. Indeed, those areas of metabolism where the enzymes involved have not been adequately examined, are those areas where our information is fragmentary and controversial. Work along these lines in recent years have revealed certain carbohydrate and protein metabolic patterns on part of Schistosoma mansoni, but the results of these studies are still inconclusive and far from being satisfactorily explained.

For better enhancement of our knowledge of the nutritional patterns of schistosomes, a more exact understanding of the specific chemically defined nutrients which these trematodes employ in their nutrition is needed. Of these nutrients, amino acids are of particular significance not only because of their role in protein synthesis, egg production and other cellular processes in which they participate, but also because of the close connection of amino acids with the metabolism of carbohydrates upon which these parasites are heavily dependant for their energy supply.

Moreover, elucidation of the amino acid requirements of the flukes would be useful, in the development of adequate chemically defined synthetic medium for their culture. In addition if it is known precisely what amino acids are required by Schistosoma mansoni and which of these could be synthesised by the organism and by what mechanisms the flukes obtain them, an opportunity might become valiable for the development of new schistosomicidal drugs.

The study of amino acid intermediary metabolism may reveal the existance of differances in the metablic activities of the worms and host tissues, and this may give promise of a rational approach to the chemotherapy of Schistosoma mansoni. Also, even in case biochemical similarites are found between schistosomes and the host, this would not preclude the possibility that the enzymes catalysing the same reactions are not identical and thus offering opportunities to develop selective antimetabolites or schistosomicides.

It is obvious that the use of adequate chemically defined synthetic medium for the in-vitro maintainance of schistosomes represents the first stage towards the determination of the amino acid requirements of these organisms. In recent years,

investigation was, therefore, focussed on the use of artificial media of known composition and approximating closely that natural environment of the parasites for the biochemical studies of these organisms. The chemically defined medium hitherto reported in literature, however, are far from being optimal as evidenced by the short-term survival of the worms and by the failure of orderly developing within the eggs. Accordingly, until this difficulty could be overcome, information on the amino acid requirments of schistosomes could be required by examining variations in the amino acid composition of the plasma of the infected host from that of the normal animal. Also, analyses of the amino acid contents of the serum culture media containing adult worms in-vitro would furnish valuable data concerning the amino acid nutritional patterns of the parasites.

The present study has been undertaken with the object of determining the quantitative changes in the amino acid composition of the horse serum medium following in-vitro incubation with adult Schistosoma mansoni worms, under very sterile conditions.

The experiment work also, involves the determination of the amino acid patterns in experimental animals (Swiss albino

mice), normal and infected with schistosomes.

In addition to this, the concentration of the free and bound amino acids content, of the adult Schistosoma mansoni, are determined.

A new all glass apparatus has been devised in the present research which has enabled the in-vitro survival of the worms up to 2 months in sterile horse serum.

Modern paper and charcoal column chromatographic techniques are employed for the quantitative amino acid analysis.

# SECTION I

# REVIEW OF LITERATURE