Potential Co - Mutagenic Risk from Treatment of Human Schistosomiasis By Praziquantel

Thesis

Submitted for Partial Fulfillment for the

Master Degree in Public Health

By

Iman Mohamed Ahmed Bakr

M. B., B. Ch.

Supervisors

Prof. Dr. Rifky Faris

Professor of Occupational Medicine

Department of Community

Environmental and Occupational Medicine

Ain Shams University

Prof. Dr. Wagida Abdel Rahman Anwar

Professor of Occupational Medicine

Department of Community

Environmental and Occupational Medicine

Ain Shams University

Faculty of Medicine

Ain Shams University

1995

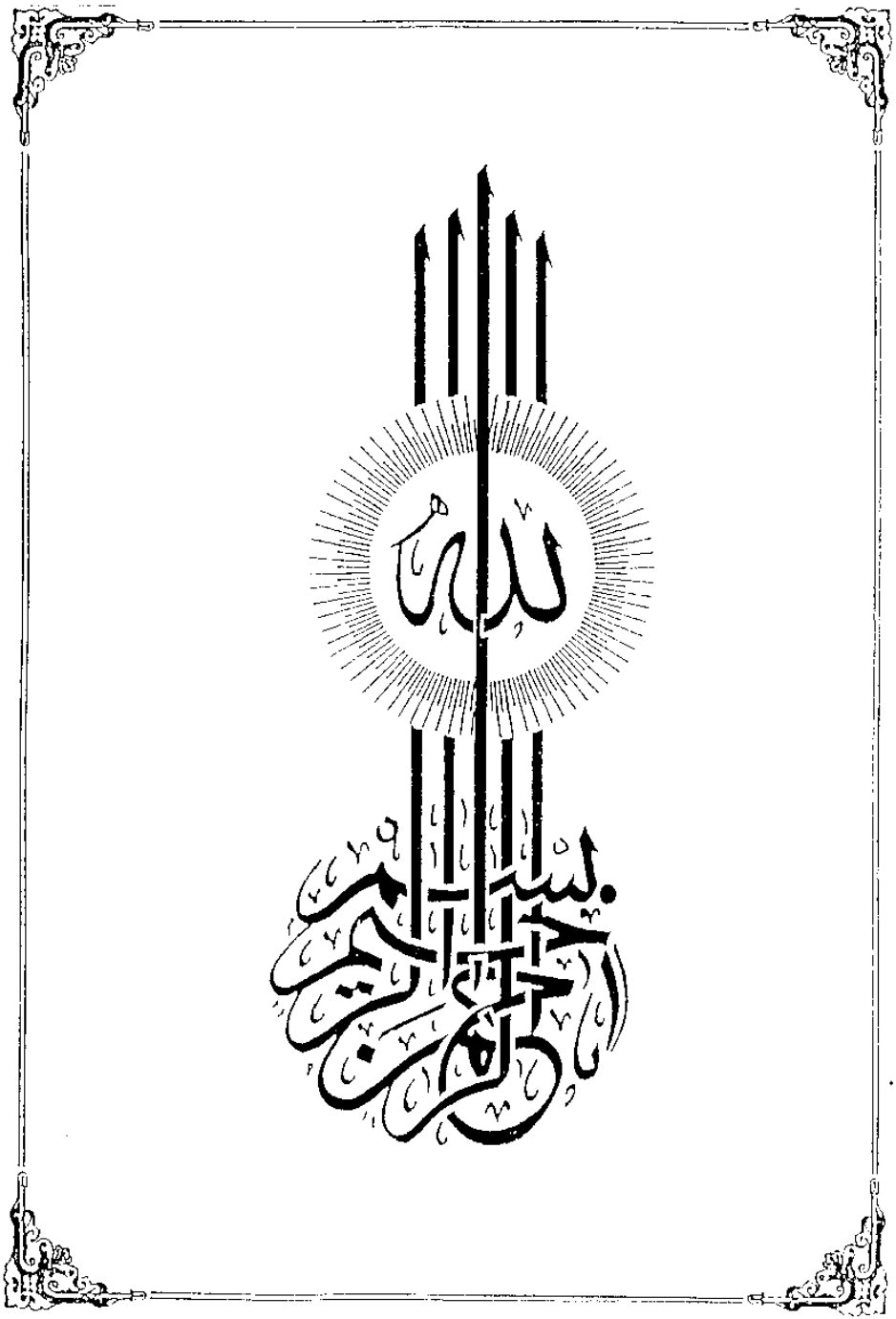
Acknowledgement

I would like to express my deepest thanks and gratitude to Prof. Dr. Refki Fares, Professor of Department of Community, Environmental and Occupational Medicine Ain Shams University, for his valuable suggestions and faithful guidance that contributed to success of the present work.

I am deeply indebted to Prof. Dr. Wagida Abdel Rahman Anwar, Professor of Department of Community, Environmental and Occupational Medicine Ain Shams University, for her generous cooperation and constructive criticism. I will always remember her sincere encouragement throughout the whole work.

I would like to thank the UNESCO Organization for the grant supplied by it for the help of this work.

To my colleagues, my family and everyone who participated in some way or another in the planning and presentation of this study in its final form.



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Aim of the work

Schistosomiasis represents one of the most common health problems in Egypt, where 21% of the population suffer from it *(Iarotski and Davis, 1981)*. It is estimated that 600 million people are at risk for Schistosomiasis, 200 million of whom are currently infected in 74 countries *(WHO, 1993)*. It is considered by the world health organization to be the second most important tropical disease *(Webbe, 1981)*.

Most of the previously used drugs for treatment of schistosomiasis were found to have mutagenic effect *(IARC, 1977)*. The question rises whether the compromised condition of the schistosomiasis patients may be responsible or can potentiate the effect of the drug ? As regards praziquantel, the widely used antibilharzial drug, it was reported lately to be mutagenic and co - mutagenic in treated mammalian cells in vivo *(Batzinger and Bueding., 1977, Shapek, et al., 1978; Feng and Seed, 1981; and Seed, et al., 1981;)*. However, in an in vivo study using micronucleus assay system in mice, praziquantel did not show any mutagenic effect, but it was co - mutagenic with high doses of Benzene (environmental carcinogen) *Anwar, et al. (1989)*.

Humans are exposed daily to multiple potentially hazardous environmental agents and drugs, however, few in vivo studies have been conducted to evaluate the genotoxic interactions between these agents.

Since the conditions of schistosomiasis patients are already compromised, their response may not be identical to that based on animal

studies. Therefore studies with appropriate human populations should be conducted to provide the needed human data to compare with the animal studies.

The Aim of this work is to study :

1 - The Cytogenetic effect of Praziquantel.

2 - The Cytogenetic effect of Schistosomiasis.

3 - The Comutagenic effects of Praziquantel with different environmental contaminents e.g. exposure to pesticides.

Review of Literature

Schistosomiasis

Schistosomiasis represents one of the most common health problems in Egypt, where 21% of the population suffer from it *(Iarotski and Davis, 1981)*. It was estimated that 600 million people were at risk for Schistosomiasis, 200 million of whom were currently infected in 74 countries *(WHO, 1993)*. It was considered by the World Health Organization to be second most important tropical disease *(Webbe, 1981)*.

Schistosomes are digenetic trematodes (flukes) belonging to the phylum platyhelminthes, they live in the blood vascular system of birds and mammals (blood flukes).

All the Schistosomes which mature in man belonged to the genus Schistosoma of the human Schistosomatidae, which contains 19 other genera, some of which were of medical importance as causes of cercarial dermatitis *(Rollinson and Southgate, 1987)*. The genus Schistosoma contains 19 species, five of which (Schistosoma haematobium, S. mansoni, S. japonicum, S. mekongi and S. intercalatum) were of major medical importance, while the others were essentially parasites of non human mammals, although some zoonotic transmission to man did ocur *(WHO, 1993)*.

Probably greater than 95% of the human cases were due to S. mansoni and S. haematobium. Several of the non human species are of veterinary importance, including S. mattheei and S. bovis, and animals were major

reservoirs of infection with S. japonicum *(Taylor, 1987).*

Life cycle :

Schistosoma do not multiply in the human body. Adult worms are found either in th vesical plexus of the bladder (S. haematobium) or in the mesenteric veins (other species), Adult worms live for a long time (up to 30 years, with a mean of 3 - 6 years) *(Anderson, 1987)* and produces a large number of eggs (300 per female per day for S. mansoni and S. haematobium and 10 times as many for S. japonicum. About one - half of the eggs transmit to the lumen of the bladder (S. haematobium) or the intestine (other species) from where they exit the body in urine or faeces, respectively. A substantial number of the eggs are retained in the tissues where they survive for a further three weeks and are responsible for including most of the pathology of disease *(Warren, 1978).*

After about 1 week in the tissues, the mature egg contains the ciliated miracidium larva, which is the life cycle stage which is infective to the snail host.

Embryonated eggs excreted from the body in urine or faeces hatch if deposited in water to liberate the free swimming miracidium larvae. If the miracidia are able to locate an appropriate type of snail host within a few hours, they penetrate the snail, if not, the miracidia (which do not feed) die.

Within the tissues of the snail, the miracidium transforms into the mother sporocyst within which are formed several hundred daughter sporocysts. They proliferate internally to produce cercariae, the stage which is infective to man. This process takes about one month, and from one miracidium several million genetically identical cercariae may be produced by this asexual process during the lifetime of the infected snail.

The cercariae are shed from the snail in response to temperature and light stimuli and aggregate at the surface of the water, ready to infect the definitive host.

They swim tail first and locate the host by a combination of chance and chemotaxis, and adhere to the skin using their suckers. Cercariae respire aerobically using glucogen as a substrate but do not feed and if they do not penetrate the final host within a few hours they die. Cercariae penetrate the skin rapidly, using proteolytic enzymes produced by paired penetrating glands at their anterier ends, the tail is discarded in the water, within the skin, a profound metamorphosis takes place and the cercariae is transformed into the skin stage schistosomulum. ***(Wilson, 1987)***.

The schistosomulum then penetrates the tough basement membrane of the epidermis, using proteinases secreted by the residual penetration glands of the cercariae stage. In mice, this process takes about 3 days after which time the schistosomulum enters a lymphatic vessel or capillary in the dermis and is carried passively to the lungs via the right side of the