GENESIS AND OBJECTIVES OF THE PRESENT STUDY

In India, like other developing and underdeveloped countries, the cardinal-most factor that accounts for poor health status and low level of economic productivity is the unhappy coexistence of innumerable parasitic infestations accompanied with generalized conditions of malnutrition.

The burden of mosquito-transmitted diseases is enormous. In addition to malaria, mosquitoes also transmit serious viral diseases (dengue, yellow fever, West Nile virus, encephalitis) and the disease caused by helminths-filariasis. Though the epidemiology of two of the above listed major diseases - Malaria and Filaria - is quite dissimilar, they have frequently combined in the same population to make the life precarious and even untenable. In developing and underdeveloped countries, worm infestation is a medical and public health problem of great magnitude both in man and his domesticated animals, directly or indirectly resulting in loss of vitality, manpower and inhibiting the economic growth of the country. The social and agricultural practices of the community as well as its sanitary habits add to the occurrence of these infections and increase in worm load.

In principle, these diseases could be controlled by eliminating the mosquitoes, but in practice this approach has serious limitations. Among the problems to this approach are the oftencited insecticide resistance and harm to the environment. Another important class of weapons in the fight against malaria/filaria is the drugs that kill the parasite in the human. The effectiveness of this approach has been limited by problems of drug resistance, cost and drug side effects. Effective vaccines have proven to be much more difficult to develop than anticipated, perhaps because during evolution the parasite has ‘learned’ how to evade the immune system. While the issue of the effectiveness of each method is debatable, there is strong consensus in the scientific community that a single approach will not be sufficient and a combination of approaches offers the greatest promise. It is in this context that the identification and inhibition of enzymes vital for the growth and survival of parasites should be viewed as a new approach for developing effective chemotherapeutic agents: the possibility of adding a new weapon to the arsenal. The work embodied in this dissertation deals with inhibition of the enzymes responsible for the biosynthesis and regeneration of Glutathione, a major tool in parasitic antioxidant defence. However, the candidate is conscious of the fact that she has touched only a fringe of the vast unchartered area of malarial and filarial biochemistry; major barriers have to be overcome before practical implementation of these discoveries can be envisioned.