Chapter I
INTRODUCTION
Malaria continues to be a major health problem in India and other tropical and sub-tropical countries of the world. Before the national antimalaria programme was started in India in 1953, the number of malaria positive cases was 75 million in the country, with as many as 800,000 deaths due to malaria. Within 5 years the antimalaria programme succeeded in bringing the malaria under control and in 1958 our National Malaria Eradication Programme (NMEP) was initiated with the assistance of World Health Organization to eradicate malaria from the country. This programme provided for a large scale distribution of conventional antimalarial drugs which was combined with insecticide spray and antilarval measures, and by 1965 this programme achieved a spectacular success and no deaths due to malaria were reported from India. However, during the last 5-7 years, there has been resurgence of malaria, and today there are more than 10 million cases positive for malaria in India alone. The World Health Organisation (1974) also expressed the opinion that it now seemed impossible to eradicate malaria from the world, and we should change the strategy of global eradication of malaria and aim at prevention of deaths from malaria.

The problem of malaria eradication is becoming more and more difficult because of the development of resistance by mosquito vectors to the conventional insecticides and the fast spread of a malignant form of malaria which is resistant to usual antimalarial drugs, is causing a serious concern in South-East Asia. In India also, NMEP has identified foci of chloroquine resistance among Plasmodium falciparum cases in Assam, Nagaland, West Bengal and some other eastern provinces. The problem is likely to be aggravated by the import of multi-resistant strains of P. falciparum from adjoining countries like Thailand, Viet Nam, Cambodia, Burma, Nepal, Bangla Desh and Sri Lanka.
In view of the tremendous magnitude of malaria problem in India, the Indian Council of Medical Research (ICMR 1977) evolved a modified malaria plan for the country, which would serve as a blue-print for future research-cum-action programme in the field of malaria in India. Studies on drug resistance in malaria have been given very high priority in the modified malaria plan and the present studies were therefore initiated to tackle various problems related to drug resistance and chemotherapy of malaria. With a view to achieve the long term objective of development of new antimalarial drugs, an active programme of large-scale screening of potential compounds for blood schizontocidal and tissue schizontocidal activity has been established in this Institute. The data presented in this thesis on chemotherapy of malaria would serve as the base line data for the chemotherapeutic activities of known antimalarials.

The present thesis deals with studies on:
(A) Chemotherapy and (B) Drug resistance in malaria.

A. Chemotherapy of Malaria

1. Standardization of rodent hosts for *Plasmodium berghei* infection.

2. Chemotherapeutic studies with known and new antimalarials and antibiotics.

3. Comparative evaluation of criteria for antimalarial activity i.e. Mean survival time, Minimum effective dose (MED) and \( \text{ED}_{50} - \text{ED}_{90} \) values.


5. Standardization of model for chemoprophylaxis (*Plasmodium gallinaceum - Aedes aegypti*).

6. Evaluation of mefloquine and antibiotics for chemoprophylaxis.
B. Drugs Resistance in Malaria

1. Selection of resistant strains of *P. berghei* to pyrimethamine, chloroquine, primaquine and mefloquine.

2. Behaviour of resistant strains in different rodent hosts.


4. Gross sensitivity of resistant strains to known and new antimalarials and antibiotics.