Preface

Parasitic infections are still one of the major health threats in the whole world. Malaria is a major parasitic disease, caused by a protozoan parasite of genus *Plasmodium*, affecting over 100 countries of the tropical and subtropical regions of the world including South-East Asia, Sub-Saharan Africa and South America. Around 300-500 million clinical cases of malaria are reported every year, and 1-3 million deaths due to complicated cases of malaria. As the available data shows that children are affected more by the disease. As per an estimate every 40 seconds a child dies of malaria. Apart from the loss of human lives, malaria is also responsible for the economic burden on the affected countries. Situation is getting worse with the emergence of multidrug resistant parasites.

The four identified species of the parasite responsible for human malaria are *Plasmodium falciparum*, *P. vivax*, *P. ovale*, and *P. malariae*. Of these, *P. falciparum* and *P. vivax* account for more than 95% of malaria cases in the world. The female anopheles mosquito transmits malaria parasites. Malaria is reemerging as the biggest infectious killer and is currently the first priority tropical disease of the WHO (World Health Organization).

The widespread development of resistance to chloroquine, the cheapest, efficacious and most widely used drug by *P. falciparum* has posed major challenges to combat malaria. Artemisinin isolated from *Artemisia annua* and its semi synthetic derivatives e.g. artemether, arteether, and artesunic acid are the only class of antimalarials, which are effective against multidrug resistant malaria. The peroxide bond in the form of 1,2, 4-trioxane is essential for the antimalarial activity of this class of drugs. Though there are not many reports of clinical resistance to artemisinin and its derivatives, yet suffer from poor oral bioavailability and high incidence of recrudescence. Also their actions are restricted to specific blood stages of *Plasmodium*.

The resistance of malaria parasite to widely used drugs prompted an upsurge in the development of new drugs with novel mechanism of action, and re-evaluation of the existing drugs to overcome the resistance problem. The work embodied in this thesis is an attempt to address this problem.

The thesis entitled “Synthesis and Antimalarial Assessment of Novel Organic Peroxides” describes our endeavors leading to the accomplishment of newer antimalarial agents. The thesis has been organized under five main chapters as summarized below:

The first chapter presents a concise review on natural products as a lead in malaria chemotherapy and accommodates some of the most significant historical achievement and development observed during the past 35 years in the discovery of antimalarial drugs.
The **chapter second** describes the synthesis and antimalarial activity of novel bis and tris-1, 2, 4-trioxanes in search for better analogue than β-arteether.

The **chapter third** of the thesis describes, whether the activity is due to the presence of two trioxane moieties or the biaryl ether moiety, we have prepared a new series of 6-(4'-aryloxy phenyl) vinyl 1, 2, 4-trioxanes and assessed them for antimalarial activity against multidrug resistant *P. yoelii* in mice by both oral and im routes. The results of this study are described in this chapter.

The **chapter fourth**, we have prepared a series of hydroxy functionalized new 1, 2, 4-trioxanes and their hemisuccinates to be used as water-soluble preparations.

The **chapter five** describes the photooxygenation of 3-(4-alkoxynaphthyl)-but-2-ene-1-ol and also describes the novel route for the synthesis of bis-1, 2, 4-trioxanes.