CHAPTER 1

INTRODUCTION

1.1. Problem Background

Malaria has been one of the most concerning global health problems. This infectious disease is caused by *Plasmodium sp.* parasite infection, carried by Anopheles mosquito as its vector (Central for Disease Control and Prevention, 2018). According to the World Health Organization (2018), there are 219 million recorded cases of *Plasmodium sp.* infection in 2017 and 435000 infected patient were reported dead. Among several *Plasmodium* species that are infective to humans, *Plasmodium falciparum* infection has been the most lethal *Plasmodium* strain. *P. falciparum* exhibits severe febrile clinical manifestation that may lead to organ failure; for instance acute renal failure, circulatory collapse, pulmonary edema, and generalized convulsions that might be followed by comatose condition and death (Mackintosh, C. L., Beeson, J. G., & Marsh, K., 2004). In Indonesia, *P. falciparum* alongside with *P. vivax* have been the most infective *Plasmodium* strain with around 12 million cases of *P. falciparum* infection occurs annually (Elyazar et al., 2011).

As a response towards this malaria infection burden, several strategies to control and eradicate malarial infection have been done within endemic areas. Out of all malaria control and eradication strategies, chemotherapy and chemoprophylaxis exhibit significant success in terms of controlling malarial infection. The discovery of Quinine as an antimalarial drug has been one of the most significant remarks in antimalarial drug discovery in the 17th century (Achan, J. et al., 2011)

1.2. Problem Formulation

Despite the tremendous success of malaria control through chemotherapy and chemoprophylaxis, there are several challenges that have been faced to eradicate malaria infection; one of the challenges is drug resistance. Alongside with the high amount of malaria

cases, current drugs that are commonly used to treat malaria, for instance, Chloroquine and Artemisinin, are also reported to undergo resistance (Bloland, P. B., 2001).

With this lack of effective drug and vaccine for malaria, the demand for a novel antimalarial drug is increasing. Several compounds which are generated chemically from either the known antiparasitic/antimalarial drugs or from chemical libraries have been one of the most promising sources for novel antimalarial drug candidate (Grimberg, B. T., & Mehlotra, R. K., 2011).

Therefore, through this study, the ability and efficacy of three O9 compound analogs: O9-03, O9-33, and O9-34 retrieved from Tokyo University Compound Library will be examined and evaluated through *in vitro* and *in vivo* assay against *Plasmodium* infection.

1.3. Research Objective

Based on the problems formulated above, the objective of this project is to determine the efficacy and affectivity of O9 compound analogs: O9-03, O9-33, and O9-34, through *in vitro* and *in vivo* assays