Artemisinin, artemether, dihydroartemisinin, and artesunic acid are able to bind to human plasma proteins [86]. In culture medium, dihydroartemisinin differentially accumulated into erythrocytes. Uninfected erythrocytes concentrated the drug less than two-fold, whereas erythrocytes infected with *P. falciparum* accumulated more than 300 times the medium concentration. The uptake process was reversible and saturable. Competition studies indicated that the receptor is the same as that for artemether. Chloroquine showed partial inhibition of uptake but was unable to release bound [$^3$H]dihydroartemisinin from infected cells [87].

An investigation of the incorporation of [$^3$H]hypoxanthine into nucleic acids of erythrocytes infected with *P. falciparum* showed a delayed inhibition by artemisinin and related compounds. It suggested that nucleic acid synthesis by *P. falciparum* was not the primary target of the drug [88]. In comparison, artemisinin, dihydroartemisinin, and artemether strongly inhibited [$^3$H]isoleucine incorporation by human erythrocytes infected with *P. falciparum*. Inhibition was observed at $\leq 1$ h after incubation with these compounds at concentrations of 50 n*M*–5 μM. Inhibition of protein synthesis exerted by these compounds may be a direct effect [89].

Para-aminobenzoic acid did not antagonize the antimalarial action of artemisinin suggesting that folic acid metabolism was not disturbed by artemisinin [65].

The structure-activity relationships of artemisinin derivatives were also studied. A series of artemisinin derivatives with antimalarial activity were subjected to quantitative structure activity relationship (QSAR) according to Hansch analysis. The log P values (octanol/waters) of various compounds, as determined by HPLC, were consistent with the additive rule of Hansch. Variations in antimalarial activities were correlated to lipid solubility. In the series of ethereal compounds, electronic parameters of various substituents significantly affected antimalarial activity [90].

An analysis using the extended Hueckel molecular orbital method revealed a linear relationship between antimalarial activity and energy levels of the fourth molecular orbital [91].

Artemisinin and some related compounds were also tested in experimental schistosomiasis and clonorchiasis. Treatment of mice infected with *Schistosoma japonicum* with either an oral artemether suspension or a s.c. oily preparation and of infected dogs orally or i.m. with artemether resulted in significant worm reduction rates [92]. In schistosomiasis infected mice intragastric administration or s.c. injection of artemether shifted all or almost all of the worms into the liver. The majority of worms that survived after intragastric treatment with artemether migrated back between days 11 and 17, while after s.c. treatment the majority were still in the liver on day 14. Artemether appeared to be ineffective against the ova [93].

Artesunate was effective against experimental schistosomiasis. When infected mice were treated orally with artesunate suspension, the total worm reduction rates were 60%–70% and the female worm reduction rates were 80%–90%. When given i.p. to infected mice, the total worm reduction rate and the female worm reduction rate were 35%–45% and 55%–75%, respectively. Artesunate also appeared to be active in rabbits infected with *S. japonicum*. It had significant activity against 1-week-old immature worms without severe side effects to infected animals [94].

Artemether at an oral dose of 300 mg/kg daily for 2 days caused degeneration of the integument, intestine, and genital gland of *S. japonicum* in the liver of host mice, achieving a potent schistosomacidal effect. Activity was more rapid and marked for