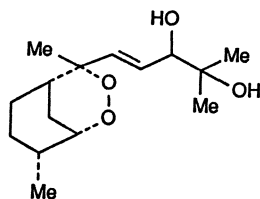


peroxide compound with antimalarial activity was isolated from *Artabotrys uncinatus* (Annonaceae), a folk medicine used in China, and named Yingzhaosu A (22-36) [59, 60].



Yingzhaosu A (22-36)

### 22.3 Pharmacology

In vitro, artemisinin was nearly as active as chloroquine against *Plasmodium falciparum* strain FCC-1/HN from Hainan island. The  $ED_{50}$  value of artemisinin and chloroquine were 1.99 and 1.24 ng/ml, respectively [61]. Klayman et al. reported that the inhibiting effect of artemisinin against *P. falciparum* in both the Camp strain (chloroquine-sensitive) and Smith strain (chloroquine-resistant) was comparable to that of mefloquine [62].

Morphological analysis of cultured *P. falciparum* treated with  $10^{-7}$ – $10^{-6}$  M artemisinin showed injury to membranes and related ultrastructure and formation of autophagocytes. There was also formation of autophagocytes but no injury to membrane ultrastructure in the presence of  $10^{-6}$  M chloroquine. Thus, the anti-malarial mode of action of artemisinin may be different from that of chloroquine [63].

In vivo, artemisinin was effective against *P. berghei* in mice ( $ED_{50}$  = 138.8 mg/kg), *P. gallinaceum* in chickens, and *P. cynomolgi* in rhesus monkeys. Intramuscular injection of an oil suspension of artemisinin was more effective than injection of a water suspension or oral administration. The oil suspension exhibited an activity similar to chloroquine in mice infected with *P. berghei* [64]. Results from experimental studies in vitro and in vivo showed that artemisinin exerts a direct parasitocidal effect on *Plasmodium* in the erythrocytic stage, whereas the parasite in the preerythrocytic stage is barely affected [65]. Microscopic examination of blood samples from mice infected with *P. berghei* and treated with artemisinin showed that after 8 h the trophozoites began to change morphologically as indicated by vacuolation, atrophy, and disappearance of the cytoplasm. After 20 h, the trophozoites showed extensive degeneration of their inner structures [65].

Rhesus monkeys infected with *P. cynomolgi* were treated with artemisinin or with chloroquine phosphate. The level of blood *P. cynomolgi* began to decrease markedly 6 h after artemisinin treatment and was undetectable after 13 h. In chloroquine treated animals the levels started to decrease after 8 h and was undetectable after 14 h. During a 10 day observation, *P. cynomolgi* reappeared in the blood of monkeys treated with artemisinin 9 days after treatment, whereas no reappearance of *P. cynomolgi* was observed in animals treated with chloroquine. The morphological