

Moreover, artemisinin was also effective in treatment of chloroquine-resistant *falciparum* malaria and cerebral malaria [74]. In general, the body temperature of patients became normal within 72 h after treatment and the asexual parasite forms were eliminated, as determined by blood films, within 120 h; however, the relapse rate within 1 month of patients treated with artemisinin was 21%. No relapse was observed in patients treated with chloroquine [74].

From a study on the effects of artemisinin and mefloquine on malaria patients infected with chloroquine-resistant *P. falciparum* it was concluded that clearance of parasitemia was more rapid with artemisinin than with mefloquine [75].

Treatment of cerebral malaria was one of the major successes of artemisinin as a new antimalarial. A clinical study of patients infected with cerebral malaria showed an average cure rate of about 90%, which was considerably higher than that of chloroquine and quinine. The time for recovery from the coma was about 21 h [74].

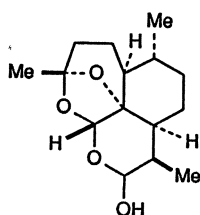
In 139 malaria patients treated with artemisinin, serum GPT activity, nonprotein nitrogen levels, and the electrocardiogram were observed before and after administration. No abnormalities were found except for a local pain at the site of injection of the aqueous suspension in some patients. Thus, artemisinin appeared to be a safe agent even in patients with complications involving heart, liver, and renal diseases or pregnancy [64, 65].

The liver appears to be the most important organ for metabolism of artemisinin. After a 1 h incubation of artemisinin with rat liver tissue 8.3% of the intact compound was recovered, kidney and lung were less active and blood was inactive. In mice, [^3H]artemisinin given orally was rapidly absorbed and the blood levels reached a maximum approximately 1 h after administration. The half-life of artemisinin was close to 4 h. About 80% of an oral dose was eliminated within 24 h [64].

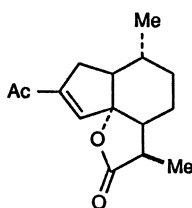
In rats, artemisinin was completely and rapidly absorbed after oral administration; however, a very low plasma level was obtained even after a dose of 300 mg/kg. When given i.m., significantly higher and more persistent plasma levels were observed. Artemisinin was shown to pass the blood-brain and blood-placenta barriers after i.v. injection. Very little unchanged artemisinin was found in the urine and feces after 48 h regardless of the administration route [76].

In dogs, after i.m. injection of artemisinin at a dose of 10 mg/kg, rapid absorption was observed with a peak serum level of 0.2 $\mu\text{g}/\text{ml}$ at 2 h and an elimination half-life of 1.6 h as detected by radioimmunoassay [77, 78].

After oral administration, four metabolites were isolated from the urines of malaria patients and healthy subjects. These metabolites were deoxyartemisinin, dihydrodeoxyartemisinin (22-37), an indenefuran derivative (22-38) [79], and 9,10-dihydroxyhydroartemisinin [80]. Artemisinin was also excreted unchanged in the feces [79].



Dihydrodeoxyartemisinin (22-37)



3,6-Dimethyl-2-oxo-8-acetyl-octahydroindene [3a, 4b] furan (22-38)