HERBCLIP

FILE: · **Sweet Annie (*Artemisia annua*)**
· **Artemisinin**
· ***Qinghaosu***

DATE: October 3, 1997 HC 100374

RE: **Review of *Qinghaosu* Antimalarial Drug from Traditional Chinese Medicine**

T.T. Hien and N. J. White. Qinghaosu. *The Lancet*, Vol. 341, pp. 603-608, March 6, 1993.

In this article, the authors provide a review of the antimalarial activity of a group of drugs derived from the Chinese medicinal herb *qing hao (Artemisia annua* L.*),* commonly known as annual or sweet wormwood. *Qing hao*'s antimalarial activity was rediscovered by the Chinese in 1971 when animal work indicated its activity against malaria parasites. Several compounds have been isolated from indigenous species of the plants, and both the parent compound and the derivatives have been shown to be considerably less toxic than chloroquine, a common antimalarial drug. The compound found to contain the principal antimalarial activity of *qing hao* was named *qinghaosu*. The western name for the compound is artemisinin. In addition to being active against *Plasmodium* parasites, artemisinin is also active *in vitro* against specific free-living amoeba and exhibits antitrematode activity against specific *Schistosoma* and *Clonorchis* organisms.

Artemisinin is effective in chloroquine-resistant cases. Responses to the herb-derived drug include a shorter parasite clearance time and a rapid reduction in malarial symptoms. The only negative observation relates to a high rate of recrudescent [recurring of symptoms after temporary abatement] infections. There has been slow progress making these compounds available outside China.

The principal active moiety of *qinghaosu* is a sesquiterpene lactone peroxide. The endoperoxide moiety is essential for the antimalarial activity and is unusual in natural products. Substitutions at the lactone carbonyl group increase potency. Oil-soluble aqueous suspensions are used for imtramuscular injections, and tablets and suppositories are also used. Dihydroartemisinin and two derivatives, artemether and artesunate, have been manufactured commercially. All three are more potent than the parent compound, but also more expensive.

Biochemical and physical properties of the most potent derivates are reviewed in this article as is the mechanism of action in parasite erythrocytes. Drug interactions that increase potency are mentioned, and the optimum time in parasitic development for treatment with the compounds is discussed. The clinical pharmacokinetics of artemisinin and several related compounds are summarized, including the expected intervals for achieving peak concentrations in the blood.

A review of clinical and comparative studies comprises half of the article. Optimum treatment doses and recommended treatment durations for *qinghaosu*, artemether, and artesunate are detailed. A brief discussion of adverse reactions mentions neurotoxicity in large animals. There have been few adverse effects. The clinical significance of a transient first-degree heart block on the third day of treatment in three patients is not clear.

Artemisinin compounds cure malaria more rapidly than other antimalarial drugs with no apparent toxicity; however, preclinical and clinical toxicity data on the compounds are insufficient to satisfy the drug regulatory requirements in many countries. While artemether is stable and can be manufactured within good manufacturing practice standards, artesunate acts more rapidly but is unstable; its manufacture falls outside of good manufacturing practice.

Artemisin suppositories are identified in this article as a major advance in the treatment of severe malaria, especially in rural locations where injections cannot be given. Combination with a longer-acting antimalarial drug gives a rapid therapeutic response while protecting the artemisinin compounds from resistance. Optimum dose regimens for the oral administration of artemisin have yet to be determined. While remarking on the lives saved, the authors strongly advise that these agents should not be given prophylactically but must be used under careful control. *—Anne Tarleton, PhD*