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Developing a Whole Plant Artemisia annua Antimalarial Therapeutic: pACT

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Et al.

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Title:
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Abstract:
The GRAS plant *Artemisia annua* L. produces the sesquiterpene lactone, artemisinin. The current therapy for malaria is artemisinin + an older drug: artemisinin combination therapy (ACT). In *Plasmodium chabaudi*-infected mice, dried leaves of *A. annua* are more potent than equal amounts of pure artemisinin and may also prevent artemisinin drug resistance from emerging. This whole plant therapy is pACT: plant-based artemisinin combination therapy. Pharmacokinetics in healthy and infected mice given either pure artemisinin or pACT is different and showed that > 40 fold more artemisinin enters the blood when plant material is present; plant matrix enhanced bioavailability into serum. Dried leaves as capsules or tablets given to African malaria patients were also efficacious. Flavonoids, phenolic acids, monoterpenes and other artemisinic metabolites found in the plant have mild antimalarial activity. Some may synergize with artemisinin to enhance its efficacy. In simulated digestion studies the effects of cellulose and gelatin capsules, sucrose, 4 oils, and 3 staple grains (rice, corn, and millet) were studied to determine their effect on AN and flavonoid release into the liquid phase of the intestinal stage of digestion. Compared to pACT alone: sucrose and oil enhanced release of flavonoids by 100%, but artemisinin was unaffected; both capsule types, and corn and millet meal significantly reduced artemisinin release, but had no effect on flavonoids. From field trials in MA, it was estimated that > 500,000 patients could be treated from plants grown on 1 ac of land. Analysis of 10 crops of the high artemisinin-producing WPI clone of *A. annua* grown under different field and lab conditions showed there was consistent production of artemisinin at about 1.4% DW. Together these results show how a simple herbal remedy could be used as an efficacious, inexpensive, controlled and sustainable orally delivered therapeutic for treating malaria and other artemisinin-susceptible diseases.

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