



Letter to the Editor

*Afr. J. Traditional,
Complementary and
Alternative Medicines*
www.africanethnomedicines.net

ISSN 0189-6016©2007

ARTEMISIA ANNUA AS A HERBAL TEA FOR MALARIA

Dear Sir,

Jansen (2006) writes that “the herbal tea approach to artemisinin as a therapy for malaria is totally misleading and should be forgotten as soon as possible.”

We believe that this statement is totally misleading and should be forgotten as soon as possible, for the following reasons.

1. The extraction method used was flawed. Boiling water will destroy most of the artemisinin, instead of extracting it, but artemisinin is better extracted in hot water (85-90°C) or milk (because of the fat content). Traditional Chinese texts suggest that the fresh juice of the plant was used (obtained by maceration and squeezing in cool water), and at much greater concentrations (Hsu, 2006). Artemisinin is stable in acid, so will survive passage through the stomach. More research is needed, using a variety of different preparations of *Artemisia annua*.
2. Dry *Artemisia annua* leaves do not lose their artemisinin fast. In proper storage conditions, the artemisinin is present in almost whole amounts even after one year of storage. Where is Dr Jansen’s scientific evidence that artemisia is susceptible to mould? Artemisinin is stored in glandular trichomes of leaves and flowers of *A. annua*. The essential oils are also stored there. Thus, fungi do not have a pleasant environment to grow in. If the plant is stored dry, the artemisinin should be there from one season to the next.
3. No one is suggesting that artemisinin is the only active ingredient in *Artemisia annua*. Jansen acknowledges that the effectiveness of the tea is partly due to other ingredients, as the dose of artemisinin is too low to account for the observed effect. This is confirmed by *in vivo* experiments in mice which showed that *A. annua* infusion reduces parasitaemia by 50% at day 4, compared to the equivalent dose of pure artemisinin, which was not significantly more effective than placebo (Plaizier-Vercammen, unpublished). The presence of other active ingredients suggests that *A. annua* is a natural artemisinin combination therapy (Willcox et al, 2004). These other ingredients also merit further research, to see whether their presence hinders the development of parasite resistance compared to pure artemisinin.
4. In the same experiments, *A. annua* infusion was less effective than the full dose of artemisinin (which was tenfold higher), suggesting that the infusion was not strong enough. The doses used by Jansen (2006), Mueller et al (2004) and R  th et al (2004) are purely arbitrary, and lower than those used in traditional chinese medicine (Hsu, 2006). Nine grams per litre is a very weak infusion: most medicinal infusions are made at the much higher strength of 50g of dried herb (or 100g of fresh herb) per litre of water (Green, 2000). If the preparations tested are insufficiently effective, the dose needs to be increased. Clinical studies in China have shown that a dose of 72-125g of *Artemisia annua* per day for three days was highly effective (Yao-de, unpublished). Experience to date and the literature suggest that *A. annua* is safe and non-toxic, though safety in pregnancy has not been established. Its LD50 is 162.5 g/kg (Chang & But, 1986). Research is needed on tenfold stronger infusions (to reach 50g of herb per litre of water) to compare their efficacy and safety with pure artemisinin at the same dose.
5. As the above statements make clear, further research is needed on *Artemisia annua* teas, to try to improve on the results obtained thus far. Important questions to address include: can the efficacy of *A. annua* tea be increased so that it becomes an acceptable complement to ACTs? How can we ensure that patients receive an adequate dose? Can *A. annua* tea be safely used without accelerating the appearance of

resistant strains of Plasmodium? It is not possible to answer these questions with a single experiment on a single preparation of *A. annua* tea.

6. While “ACTs for all” would be the ideal strategy, it is most impractical for poor and remote communities, politically unstable areas, and people who dislike the use of modern medicine. There are almost five billion febrile episodes resembling malaria every year (Breman et al, 2004), most of which need to be treated as malaria, since most areas do not have adequate diagnostic facilities. Even at the cost of \$1 per course of treatment (which is half the current price of ACTs) this would cost almost \$5 billion per year, which is ten times the currently available budget for malaria. Even if this money miraculously appeared, the health infrastructure is lacking in most of the areas worst affected by malaria, making it impossible to distribute the drugs to those who most need them. For example, in the Brazilian Amazon, patients commonly have to travel for two days before reaching a modern health facility. Although recrudescence can occur after treatment with *Artemisia annua* tea, is this not preferable to patients dying before they reach the health facility? Why not recommend the tea as a “first aid” measure to keep the patient alive while they travel to the health centre?

It is clear that further concerted research is needed to optimise the dose and preparation of *A. annua* (including combinations with other antimalarial plants), to tackle the problem of recrudescence, and to conduct trials in non-immune populations. If these show sufficient effectiveness, a sustainable treatment for malaria could be made available to those in remote areas who cannot rapidly access modern health care. If the herbal approach is “forgotten”, those remote populations will also remain forgotten. In any case, they cannot access the products of the pharmaceutical industry, so it need not feel threatened by this approach. There is one point where *A. annua* herbal preparations will never reach the efficiency of pure artemisinin: ...business, of course!

Yours sincerely,

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