Inhibitory activity of plant extracts on Plasmodium falciparum aquaporin

J. Pei and A.J. Yool, Discipline of Physiology, School of Medical Sciences, University of Adelaide, SA 5005, Australia.

Malaria is one of the top three global infectious diseases that are life threatening. In 2002, there were about 300-600 million malaria cases recorded globally (Snow et al., 2005). For humans, Plasmodium falciparum accounts for most of the severe and fatal malaria cases. Plasmodium falciparum aquaglycerolporin (PfAQP) is expressed on the parasite plasma membrane which is the major glycerol transporter (Beitz, 2007). Mice infected with PfAQP knockout parasites had a longer survival time compared with wildtype parasites (Promeneur et al., 2007). Because the mutation rate of PfAQP gene is relatively low compared with the majority of the genome (Bahamontes-Rosa et al., 2007), a PfAQP blocker could be a good goal for anti-malarial drug development. I hypothesized that these plants, Bacopa (Bacopa monnieri,), Rhubarb (Rheum rhuababarum), Ginseng (Panax ginseng) and Fuling (Poria cocos), that have been used as diuretics in traditional medicine have an inhibitory effect on PfAQP. Xenopus laevis oocytes that express PfAQP were used in the swelling-shrinking assays to test the inhibitory effect on PfAQP of selected plant extracts. Two hours incubation in three of the whole plant extracts (5mg mL^{-1}) decrease the glycerol swelling rate to 7.16%, 7.37% and 20.01% respectively compared with the swelling rates of untreated oocytes. Plant extracts were fractionated by reverse-phase chromatography using C18 silica column and mobile phase of 100% to 0% water in methanol. Six fractions were collected and dried down. Active fractions inhibited the glycerol permeability of PfAQP dose dependently and the inhibitory magnitude increased with time. Chemical analyses of the active components are in progress. The identification of first plant derived PfAQP blockers present exciting opportunities for the development of novel anti-malarial drugs.

- Bahamontes-Rosa N, Wu B, Beitz E, Kremsner PG, Kun JF. (2007) Limited genetic diversity of the Plasmodium falciparum aquaglyceroporin gene. *Molecular and Biochemical Parasitology* **156**: 255-257.
- Beitz E. (2007) Jammed traffic impedes parasite growth. *Proceedings of the National Academy of Sciences of the USA* **104:** 13855-13856.
- Promeneur D, Liu Y, Maciel J, Agre P, King LS, Kumar N. (2007) Aquaglyceroporin PbAQP during intraerythrocytic development of the malaria parasite Plasmodium berghei. *Proceedings of the National Academy of Sciences of the USA* **104:** 2211-2216.
- Snow RW, Guerra CA, Noor AM. Myint HY, Hay SI. (2005) The global distribution of clinical episodes of *Plasmodium falciparum* malaria. *Nature* **434**: 214-217.