



January 31, 2008. Malaria-Infected Mice Are Cured by Oral Administration of New Artemisinin Derivatives

Johns Hopkins Malaria Research Institute researchers have cured malaria-infected mice with three low oral doses of a new series of potent, long lasting synthetic drugs modeled on the ancient Chinese herbal drug artemisinin. An article about the team's work appeared online on January 31, 2008 in the ASAP section of The Journal of Medicinal Chemistry.

In four or five chemical steps from the 1,2,4-trioxane artemisinin, a new series of 23 trioxane dimers has been prepared. Eleven of these new trioxane dimers cure malaria-infected mice via oral dosing at 3×30 mg/kg. The clinically used trioxane drug sodium artesunate prolonged mouse average survival to 7.2 days with this oral dose regimen. In comparison, animals receiving no drug die typically on day 6–7 postinfection. At only 3×10 mg/kg oral dosing, seven dimers prolong the lifetime of malaria-infected mice to days 14–17, more than double the chemotherapeutic effect of sodium artesunate. Ten new trioxane dimers at only a single oral dose of 30 mg/kg prolong mouse average survival to days 8.7–13.7.

These peroxide compounds, containing a crucial oxygen-oxygen unit, promise not only to be more effective than today's best malaria remedies, but also potentially safer and more efficient, said research team leader Gary Posner, Scowe Professor of Chemistry in the Krieger School of Arts and Sciences at Johns Hopkins.

Since 1992, Posner and his team, which includes collaborator Theresa Shapiro, professor and chair of clinical pharmacology at the Johns Hopkins School of Medicine, have been tackling that challenge by designing a series of peroxide compounds, called trioxanes.

The Johns Hopkins trioxanes mimic artemisinin, the active agent in a Chinese herbal drug used to treat malaria and other fevers for thousands of years. Artemisinin comes from the *Artemisia annua* plant, an herb also known by a variety of names including sweet wormwood.

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