

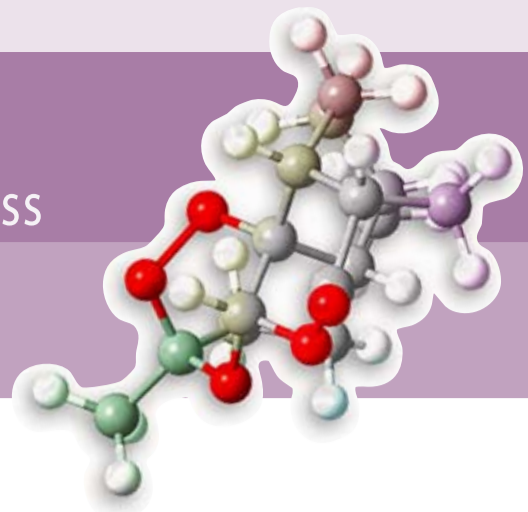
THE ARTEMISININ ENTERPRISE

New Sources of Artemisinin to Reduce Economic Barriers to ACT Access

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Background

The World Health Organization recommends artemisinin combination therapies (ACTs) as the first-line treatment for malaria, a policy adopted by 75 countries^{1,2}. However, ACTs are more expensive than the drugs they are replacing and this is a major barrier to their effective deployment^{3,4}.

Artemisinin production represents a significant proportion of the manufacturing cost of ACTs⁵. The price of artemisinin is extremely volatile and quality is variable. Artemisinin is derived from the medicinal plant *Artemisia annua*, but yields from the plant are low and supplies are uneven. The projects in the Artemisinin Enterprise share the ultimate goal of making high-quality ACTs less expensive and more accessible to the people who need them.



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The Artemisinin Enterprise

The Artemisinin Enterprise comprises three complementary scientific projects with support from the Bill & Melinda Gates Foundation. Its aim is to improve artemisinin production technologies, which should;

- diversify the sources of high quality artemisinin,
- lower the cost of artemisinin production,
- stabilize supplies, preventing cyclical fluctuations in artemisinin prices,
- provide new antimalarial combinations,
- make high-quality ACTs less expensive and therefore more accessible.

Impact of the new technologies

Products from the Artemisinin Enterprise are anticipated to enter the market from 2010. All three approaches are needed to satisfy projected global demand for ACTs. The projects are collaborating for maximum impact on ACT supply chains and to ensure the new technologies do not enter substandard drug or monotherapy supply chains.

Lowering artemisinin production costs with these new technologies should improve the artemisinin supply such that ACT prices fall significantly. Furthermore, diversifying the sources of artemisinin will help stabilize supplies, preventing cyclical fluctuations in artemisinin prices. To make affordable ACTs available to those who need them, other supply chain problems such as stability, leakage to the black market, counterfeiting, distribution, and private sector regulation must also be addressed.

Successful delivery of the Artemisinin Enterprise projects will make an important contribution to the provision of affordable ACTs and new malaria therapeutic options, whilst providing incentives for existing *Artemisia* growers and artemisinin manufacturers to remain in the market.



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Semisynthetic artemisinin through fermentation



A partnership of the Institute for OneWorld Health, University of California, Berkeley, and Amyris Biotechnologies, called the Artemisinin Project, is using synthetic biology and classic chemistry techniques to develop semisynthetic artemisinin. The biological stage employs an engineered microbe to convert simple sugars into artemisinic acid using microbial fermentation. Several chemical synthesis steps then convert artemisinic acid into artemisinin. The project aims to create, optimize, scale-up, and industrialize microbial production systems to make bulk artemisinin available for incorporation into ACTs, at a low price with consistent high quality. Currently in the third year of a five-year development effort, this project aims to incorporate semisynthetic artemisinin into at least one high quality ACT by 2010-2012.

Fast-track breeding of Artemisia



The Centre for Novel Agricultural Products (CNAP) at the University of York is applying fast-track breeding technologies to Artemisia with the aim of creating new, non-genetically modified (GM) varieties with increased artemisinin yields. Many thousands of plants are being screened at both the phenotypic (trait) and genetic levels. Promising individuals will be used in a classical crop breeding programme to create new varieties. Seeds will be made available at cost to the ACT supply chain. The Swiss not-for-profit organization, Médiplant is collaborating with plant breeding and roll-out.

A new class of synthetic peroxides



The artemisinin molecule contains a peroxide chemical bond, which is believed to be essential to its anti-malarial activity. The not-for-profit organization Medicines for Malaria Venture (MMV) is collaborating with a number of research partners including the University of Nebraska, Monash University, and the Swiss Tropical Institute, on the development of a new class of antimalarial compounds, dubbed the 'Next Generation Oz' that have a similar peroxide moiety. The team is now testing these compounds to find drug candidates that could potentially have a different mode of action or molecular target in the *Plasmodium* parasite compared with artemisinin.

References

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- (5) Hale, Victoria, Keasling, Jay, Renninger, Neil, Diagana, Thierry, Microbially Derived Artemisinin: A Biotechnology Solution to the Global Problem of Access to Affordable Antimalarial Drugs. American Journal of Tropical Medicine & Hygiene. 2006: October 13.