appeared on 19th Apr 2006

New anti-malarials in the brew

A new role of wine yeast may be to help bring malaria under control, says S.Ananthanaryanan.

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The use of ***Saccharomyses cerevisiae***, or wine yeast, in making wine is probably the earliest bio-based industry known to humankind. Now bio-engineering has made use of this same organism to synthesize a complex natural substance which has the remarkable quality of controlling cerebral Malaria!

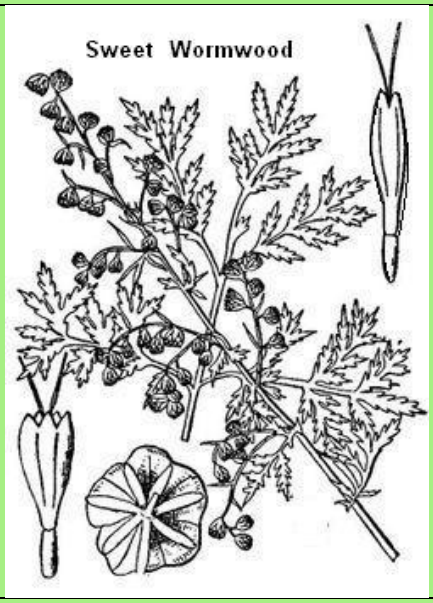
Malaria parasites

Malaria has been a scourge throughout history and has killed more people than all wars and other plagues combined. It is considered the most important parasitic disease that affects humans - almost 500 million people are affected and 2.7 million are killed each year. – and 90% of the victims are children.

The disease, which first affects the blood cells and then leads to multiple organ failure, is caused by two main strains of parasite – plasmodium vivax and plasmodium falciparum. The first is the most common, but the second affects the blood supply to the brain and is by far the more deadly.

While treatment with quinine was the standard, and some more remedies have been developed, a problem of late is that the parasite, particularly the falciparum strain, has become resistant to even multi-drug attacks. Synthetic drugs and vaccines are under development but are yet to be perfected and tested.

Anti-malarial plant



A ray of hope is the discovery that artemisia annua (commonly known as Sweet Wormwood, Sweet Annie or Chinese Wormwopod) contains agents that are remarkably effective against malaria. The plant, which has fern-like leaves, bright yellow flowers and a camphor-like scent, was traditionally grown in China (and now in Europe and India) and was long used by Chinese herbalists for several diseases, including malaria, apart from its use in the perfumery industry. Research in China has now revealed that *A. annua* yields a compound *qinghaosu* or artemisinin, which has potent anti-malarial action with little or no side effects The plant can be grown on hills and plateaux, where the climate is temperate-like, and good yields can be obtained in five to six months.

A.annua has been introduced in African countries, but the problem is that the quantity of the drug from the plants that can be extracted is low and supply is far short of needs. The drug is thus both scarce and too expensive for the most vulnerable populations.

This is where the work of Jay Keasling and others at the Univ of California at Berkley may become important.

Bio-engineered yeast

Although synthesis, from scratch, of artemisinin is difficult and costly, preparation from artesiminc acid, its precursor, is both economical and effective. The group at Berkley has worked on engineering metabolic pathways to create this precursor, artesiminc acid by mimicking the biosynthesis route that is used by the sweet wormwood plant. Plants and herbs like the wormwood and various micro-organisms synthesise an incredible diversity of complex chemicals. Analyses and replication of the synthesis scaffolding that these factories of complexity contain could lead to mechanisms to manufacture in large quantity a great variety of reactants that it is otherwise impossible to put together.

Jay Keasling's group in Berkley has succeeded in introducing in the cell of wine yeast, s*accharomyses cerevisiae*, the genes in artemisia annua which bring about the construction of artemisinic acid. It is then feasible to create sizeable quantities of this raw material for preparing or artemisinin, the potent anti-malerial, using a fermentation bath populated with the genetic engineered yeast cells. The achievement, reported in ***Nature***, last week, is said to be ready for industrial scale up.

The technique also opens the door to using genetically redesigned cells for inexpensive and ecologically acceptable production of a number of vital drugs, some used to treat cancers, which are otherwise derived only from plants.