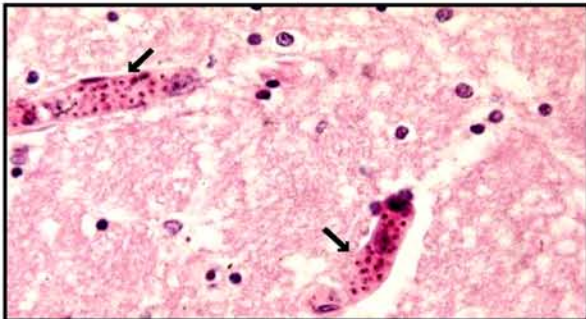


Cerebral Malaria

Cerebral malaria (CM) is the most common complication and cause of death in severe *Plasmodium falciparum* infection. In *falciparum* malaria, 10% of all admissions and 80% of deaths are due to the central nervous system (C.N.S.) involvement. It is an acute, widespread disease of the brain, which is accompanied by fever. The mortality ratio is between 25-50%. If a person is not treated, CM is fatal in 24-72 hours. Manifestations of cerebral dysfunction include any degree of impaired consciousness, delirium, abnormal neurological signs, and focal and generalized convulsions. In severe *P. falciparum* malaria, the neurological dysfunction can manifest suddenly following a generalized seizure or gradually over a period of hours.

Death from severe malaria in children is most often caused by cerebral malaria, severe malarial anemia, acidosis with accompanying respiratory distress, or a combination of these factors. Cerebral malaria is associated with a particularly high mortality rate, which averaged 18.6% in a 1998 survey of studies of African children.

Chemotherapy for cerebral malaria now primarily involves the use of quinine, for a patient with severe CM must be assumed to have chloroquine resistance. It is one of the four main alkaloids found in the bark of the Cinchona tree and is the only drug which over a long period of time has remained largely effective for treating the disease. Artemisinins have been shown in some clinical trials to clear parasitemia and fever faster than quinine or chloroquine.



Section of the brain showing blood vessels blocked with developing *P. falciparum* parasites (see arrows)

Bioresonant Phytotherapeutics

Bioponic Phytoceuticals is a pioneer in the discovery and development of a new natural healing modality called "bioresonant phytotherapeutics". This healing methodology utilizes the process of tuned sympathetic bioresonance which is produced in the molecular memory of condensed water molecules, entrained with the phytochemical signature of the distilled herbal plant. This establishes a bioresonant harmonic within the phytotherapeutic, which in turn provides healing through optimum bioavailability. The principle of sympathetic resonance states that if there are two similar objects, and one of them is vibrating, the other will begin to vibrate as well.



Biophysicists view the body as an interconnected bio-energetic organism. The key to understanding bioresonance lies in understanding the fact that all vital processes in the organism are influenced and controlled by electromagnetic oscillations. Bioresonance provides the mechanism for electron communication and interaction that is the catalyst for all biochemical processes. Resonant frequencies travel through the body along cell membranes, through bi-polar water molecule chains, along protein chains, and through the electrolyte rich connective tissue reaching every part of the body.

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Curemisiin™

Bioresonant Phytotherapeutic
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(Remedy for Malaria)

Malaria

Malaria is one of the most important global health problems, potentially affecting more than one third of the world's population. Currently, malaria has been found resistant to many first and second line allopathic drugs. An article published in *Infections in Medicine*® "Cerebral Malaria in Children" by Chandy C. John, MD, MS, Richard I. Idro, MBChB, MMed, states "*Plasmodium falciparum* malaria is a leading infectious cause of morbidity and mortality in children worldwide. Each year, 300 to 500 million clinical cases of malaria occur, resulting in 1.5 to 2.7 million deaths. Most deaths caused by malaria occur in children younger than 5 years in sub-Saharan Africa." In India more than 2 million people are afflicted with malaria leading to morbidity, loss of man-hours, and economic loss. This requires the continuous development of potential new antimalarial products. Combinations of antimalarial compounds, which have different molecular targets, delay the emergence of resistance.



Malaria parasites are transmitted from one person to another by the female anopheline mosquito. *Plasmodium* develops in the gut of the mosquito and is passed on in the saliva of an infected insect each time it takes a new blood meal. The parasites are then carried by the blood in the victim's liver where they invade the cells and multiply.

Curemisinin™ uses a "combination of natural products" approach by combining the anti-malarial effects of known (and currently utilized) effective herbal agents: *Artemisia* (source of artemisinin), Turmeric root (source of curcumin) and *Cinchona* bark (source of natural quinine alkaloids). In combination, this formulation offers a useful remedy to address the problems of malaria. In addition, Bioponic Phytoceuticals' use of a nasal delivery system allows the liquid remedy to be delivered directly to the brain via the nasal membrane. This may have a significant impact on Cerebral Malaria, a condition that especially affects children and is deadly if not treated.

Artemisinin

Artemisinin is a compound used to treat multi-drug resistant strains of *falciparum* malaria. The compound is found in the shrub *Artemisia annua* and is used in traditional Chinese medicine. In China during 1979, Artemisinin trials were conducted wherein 2,099 patients infected with *P. viva* and *P. falciparum* were tested. Artemisinin had good therapeutic effects and improved or cured all patients. Furthermore, the treatment with Artemisinin was without any obvious side effects. Artemisinin is also effective in cerebral malaria. Body temperature of patients normalized within 72 hours, and asexual parasites were eliminated within 72 hours. Mutations conferring resistance to artemisinins have never been documented and are therefore much less likely to occur than mutations to some other drugs. Artemisinins are a particularly effective partner drug because they are more active than any other antimalarial. In addition, artemisinins have broad stage specificity and can be used to treat severe as well as uncomplicated malaria. The World Health Organisation has recommended that a switch to Artemisinin Combined Therapies (ACT) should be made in all countries where the malaria parasite has developed resistance to chloroquine.

Curcumin, a compound isolated from the turmeric plant, has been found to possess qualities that can effectively fight malarial parasites, including the dreaded drug-resistant forms of *Plasmodium falciparum* or cerebral malaria, according to the intensive study being carried out by scientists of the Department of Biochemistry, Indian Institute of Science at Bangalore. Prof G Padmanabhan and his team found that treatment with a Curcumin based combination leads to complete clearance of parasites in blood and total protection against mortality in experimental animals. Scientists at the Indian Institute of Science (IISc) in Bangalore and the University of Michigan Medical School, United States have shown that curcumin inhibits drug resistant forms of *P. falciparum*. The findings have been published in *Biochemical and Biophysical Research Communications* in January 2005. (Reddy RC, Vatsala PG, Keshamouni VG, Padmanaban G, Rangarajan PN. Curcumin for malaria therapy. *Biochemical and Biophysical Research Communications*. 2005;326(2):472- 474).

Artemisinin and Curcumin

The rationale for using compounds in combination is well established. The probability of a parasite arising that is resistant simultaneously to multiple compounds with unrelated modes of action is the product of the per parasite mutation frequencies multiplied by the total number of parasites exposed to the compounds. Artemisinin and Curcumin show an additive interaction in killing *Plasmodium falciparum*. Artemisinin derivative-based combination therapy (ACT) has been advocated as the therapy of choice to handle widespread drug resistance in *Plasmodium falciparum* malaria, at the same time preventing recrudescence due to artemisinin monotherapy. The curcumin-artemisinin combination may prove superior from several perspectives. Both are from natural sources of long-term use, and no resistance is known to curcumin.

In a paper published in *Antimicrobial Agents and Chemotherapy* journal, Padmanaban and Rangarajan along with D.N. Nandakumar, P.G. Vathsala and V.A. Nagaraj said the advantage of the combination was manifold. Both were derived from natural sources so were free from side-effects and toxicity. Curcumin is tolerated at very high doses. With the malaria parasite developing resistance to first line and second line drugs like chloroquine and antifolates, artemisinin and its derivatives have remained the only treatment options.

Cinchona Bark

(*Quinaquina officinalis*, *Quinaquina lancifolia*, *Quinaquina coccinea*) Natural quinine compounds extracted from *Cinchona* are making a comeback in the management and treatment of malaria. Malaria strains have evolved which have developed a resistance to the synthesized quinine drugs. It was shown in early studies that an effective dose of natural cinchona bark extract elicited the same antimalarial activity as an effective dose of the synthesized quinine drug. Scientists are now finding that these new strains of drug-resistant malaria can be treated effectively with natural cinchona bark extracts. As evolving pathogens develop widespread resistance to our standard antibiotics, antivirals, and antimalarial drugs, the use of the natural medicine in cinchona bark is being revisited, even by the World Health Organization.