

FEATURED ARTICLES

African Traditional Herbal Medicine in the Management of Chronic and Acute Malaria

By Nakato & Kiwanuka Lewis

Blackherbals at the Source of the Nile UG, Ltd.
African Traditional Herbal Research Centre/Clinic

Abstract

Gloria, a 15 year old student with chronic malaria and epilepsy, was presented to the African Traditional Herbal Research Clinic after medical doctors had given up on the available treatment. The African Traditional Herbal Research Clinic in Kampala, Uganda is headed by two Diasporans, an herbal technologist and a research chemist. We use African traditional herbal methods guided by western diagnostics as the means of managing chronic diseases. Gloria's father appealed to the traditional health community for assistance after all other methods had failed. We responded. The result is that Gloria has been attending school for the past two years with no attacks of malaria or from epilepsy.

Key Words: cerebral malaria, acute and chronic malaria, epilepsy, herbal anti-malarials

Introduction

Malaria, the ancient mosquito-borne disease that was "rolled back" by medical advances in the mid-20th century, has made a deadly comeback. Infectious strains of the disease are becoming increasingly resistant to treatment, infecting and killing more people than ever before, sickening as many as 900 million worldwide in 2003. More than 1 million people and by some estimates, as high as 2.7 million of those victims died. The vast majority of the deaths were in Africa. Among children, malaria kills even more than AIDS. One of the major causes of malaria's alarming resurgence is the parasite's increasing resistance to the pharmaceutical drugs used to treat and prevent the disease. Chloroquine, the cheapest and most effective anti-malarial since the 1950's have become ineffective in up to 80 percent of malaria cases in some countries.

Chloroquine and Fansidar (sulphadoxine-pyremethamine (SP)) were dropped by the government of Uganda as the main drugs in the treatment of malaria on advice of the

World Health Organisation, following research showing that malaria parasites had grown highly resistant to the medicine. Leaving behind Chloroquine and Fansidar, the health ministry in Uganda adopted Artemisinin Combination Therapies (ACT) and as part of that change of policy the government introduced Coartem as an ACT therapy which combines two drugs Artemether and Lumefantrine. However, a new form of malaria discovered in Cambodia is more resistant to the drug artemisinin and has been spreading rapidly in the region, causing concern that it could spread globally.

In Africa, the economic cost of malaria in manpower and human life is very high. Current techniques used to control the disease include mosquito eradication with insecticides, prevention of mosquito bites, and the use of drugs to prevent and treat infection.

Malaria in humans is caused by a protozoan of the genus Plasmodium consisting of five species, falciparum, vivax, malariae, ovale, and knowlesi. All five species are present in sub-Saharan Africa. Most infections in Uganda are caused by Plasmodium falciparum and P. knowlesi. Death is caused almost exclusively by the former.

Falciparum, the most common cause of acute infection, is responsible for about 80% of all malaria cases, and is also responsible for about 90% of the deaths from malaria. The latter species cause an acute and chronic form of malaria that is recurrent in the infected patient (causing bouts of disease long after the original infection). However, differences in racial distribution, (genotype/phenotype) or in blood groups do confer some resistance, (e.g. lack of Duffy antigens in blacks to P. vivax in 68% African Americans and 88–100% in Africans, including more than 90% of West Africans). This phenotype is exceedingly rare in whites.

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The disease is transmitted by the bites of mosquitoes of genus *Anopheles*, of which the *Anopheles gambiae* complex is mainly responsible for the transmission of disease in Africa. The parasites are transmitted from one individual to the next by mosquito bites. The life cycle thus consists of a mosquito stage and a human stage. In chronic malaria there are also two main stages in the human, first in the liver and then in the blood and other organs. The liver stage, which has no symptoms, lasts about a week to ten days after the bite of the infected mosquito. Thereafter the parasites emerge into the blood, with the onset of symptoms. Present malaria pharmaceuticals are therefore directed at the blood stage.

The most severe manifestations are cerebral malaria (mainly in children and persons without previous immunity), anemia (mainly in children, pregnant women and people with HIV), kidney and other organ dysfunctions (e.g., respiratory distress syndrome). Symptoms include high fever, severe headache, parasitemia, intense cold or heat, chills, drowsiness, unconsciousness, seizures, delirium, and confusion. Although much work has gone into developing malaria vaccines, the availability of a vaccine, by WHO estimates, is still years away.

Side Effects of Antimalarial Drugs

Some of the more severe side effects associated with antimalarial medications is psychiatric in nature. For example, the drug mefloquine (Lariam, Hoffman-La Roche) has been reported to cause nightmares, hallucinations and other confused behavior. Having thoughts of suicide and seizures are other severe side effects and people with known psychiatric illness and epilepsy should avoid using this medication. More common Lariam side effects include nausea, vomiting, diarrhea, abdominal pain, dizziness, vertigo, sleep disorders, ringing in the ears, headache, muscle cramps, abnormal dreams, emotional instability, insomnia, panic attacks, hallucinations, anxiety, depression, paranoid reactions, convulsions, visual impairment, numbness, rashes, and itching.

Quinine, has the potential to cause toxic reactions to structures of the inner ear, including the cochlea, vestibule, semicircular canals, and otoliths, and is considered ototoxic. Drug-induced damage to these structures of the auditory and balance system can result in hearing loss, tinnitus, and dysequilibrium or dizziness. Nervous system side effects have included apprehension, restlessness, confusion, syncope, dizziness, vertigo, tinnitus, hearing loss, and nystagmus (involuntary eye movement).

Cinchonism (pathological condition in humans caused by

an overdose of quinine or its natural source, cinchona bark) has been reported with repeated doses or high serum levels in 25% to 100% of patients. The clinical presentation of cinchonism have included temporary deafness/slight deafness, tinnitus, headache, dizziness, rash, mental dullness, depression, confusion, and nausea. Fatalities have been reported from single oral doses of 2 to 8 grams.

Hemolytic anemia, usually a result of G6PD deficiency, is a serious side effect of several antimalarial drugs, including quinine. (G6PD deficiency is an inherited condition in which the body doesn't have enough of the enzyme glucose-6-phosphate dehydrogenase, or G6PD, which helps red blood cells (RBCs) function normally.) Cardiac issues like heart arrhythmias, weak pulse and EKG irregularities are severe side effects that can also result from quinine.

Malarone (atovaquone and proguanil) is one of many drugs implicated in the severe, life threatening skin disease known as Stevens-Johnson syndrome. Severe skin rashes and uncontrolled diarrhea and vomiting are serious side effects to include possible bleeding disorders. Pregnant women should not be treated with some antimalarials because of potential birth defects.

Almost all antimalarial drugs cause some gastrointestinal (GI) disturbance, which can include nausea, vomiting, diarrhea, loss of appetite, mild weight loss, light-headedness and dizziness. General side effects such as headaches, coughs, rashes and general weakness can also be a result of any of the antimalarial drugs. Most antimalarial western drugs do not prevent malaria.

Current Research

Chemical eradication of the mosquito population in Africa is of major importance in controlling outbreaks of malaria. *Anopheles* mosquitoes have become resistant to most chemical insecticides to the point that only DDT (since it was not used previously in Africa for malaria eradication) remains effective in controlling the insect population. DDT is banned in North America, Western Europe and other industrialized countries because of its purported dangers to human and environmental health.

Recently, the World Health Organisation reversed the ban on DDT so it could be used for indoor spraying of mosquitoes in malaria-endemic areas. The long term effects of DDT on agriculture, the environment and human health are downplayed. DDT has been found to cause a number of health problems, in addition to its known environmental hazards. Some of the more recent scientific findings on DDT include damage to the developing brain, hypersensitivity, behavioral abnormalities; reduce neural signal transmission,

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endocrine disruption, diabetes, early puberty, premature births and low birth weight, learning disabilities, low IQ, and suppressed immune systems resulting in slower response to infections. Scientific investigations of recent DDT use in Mexico and South Africa reveal that human breast milk containing DDE (the breakdown product of DDT) are at concentrations that exceed the acceptable guidelines for intake set by the WHO.

Current anti-malarial drugs have their share of problems as well. Chloroquine remains the first-line drug of choice in most of sub-Saharan Africa, although its resistance in some areas is as high as 80%. Resistance has been spreading westward, attaining levels of 20% to 35% in West Africa. The alarming increase in resistance in eastern and southern Africa requires that sulfadoxine-pyrimethamine (Fansidar, Hoffman la Roche) replace chloroquine as the first-line drug. Resistance to mefloquine, another first-line drug, developed in the early 1980's, was noticed soon after its introduction and is now almost at the same level as chloroquine. Sufadoxine-pyrimethamine is the second line drug in many countries of West and Central Africa, but so much resistance appears to be rising in countries of East Africa that atovaquone/dapsone (Malarone, Glaxo Wellcome) was developed as a replacement. Other drugs used in Uganda include Homapack, Coatem, Lumartem, and Falcimon Kit.

Although resistance is increasing, intravenous quinine is still the main therapy for cerebral malaria and vaccines for malaria are still under development. WHO has stated there are no viable vaccines. Many herbalists and other health care professionals consider vaccinations to be the introduction of disease where none existed. But this is where most of the present malaria research is headed. The types of vaccines currently under development include recombinant, genetically modified plasmodium clones.

Artemisinin (*Artemisa* spp.) and pyrethrum (*Chrysanthemum cinerifolium*) are two herbal plants overwhelmingly approved for use in the treatment of malaria and its insect vectors, but it is recommended that these be used in combination with pharmaceuticals (ACTs) and pesticide chemicals (pyrethroids) to control resistance. Bed-nets, impregnated with pyrethroids, can cause additional medical problems. Pyrethroids are absorbed across the skin barrier through melanin, through the lungs and through the gut. They can cause such medical problems as allergies, asthma, contact dermatitis, gastric disturbances, neurological and reproductive problems and lower body immune functions, to name a few. Pyrethroid resistance has been reported in *An. gambiae* in West Africa and there is concern about its

emergence in E. Africa.

Studies undertaken in Kenya by the International Center of Insect Physiology and Ecology (ICIPE), on the use of traditional medicine in malaria and mosquito control, are rediscovering and improving on traditional methods adopted by communities in East Africa and elsewhere to reduce the human-mosquito contact. Many communities have traditionally developed the knowledge that hanging leaves of certain plants on doorways, or burning certain plants and cow dung are effective deterrents against mosquitoes. For instance, the Kamba, Swahili and Luo communities had identified such plants as mwenye and kirumbasi (*Ocimum basilicum* L), and mukandu (*Ocimum gratissimum*) as effective fumigants. By hanging branches from the trees on doorways and on windows, they were able to prevent mosquitoes from entering their dwellings. Today, the Swahili people still burn kirumbasi in small jikos to produce mosquito-repelling incense.

In contrast, the UN is attempting to harness nuclear technology to try to eradicate the mosquitoes. The International Atomic Energy has developed the "Sterile Insect Technique" where scientists are breeding insects and exposing the males to enough radiation to render them sterile. The males are then released into the environment to breed with the females, whose eggs are unfertilized and will never hatch. The concept is based on the depopulation of the mosquito leading to its eradication and subsequently to the eradication of the disease.

The genome sequences of the plasmodium parasite (2002), the *An. gambiae* mosquito (2002) and man (2004) have been published. In 2000, scientists successfully inserted a functional gene into malaria-transmitting mosquitoes. This was a breakthrough in malaria research. The gene made the mosquito glow green under ultraviolet light. They hoped to replace this gene with a gene that inhibits development of the malaria parasite. The ability to introduce foreign genes into *Anopheles* vectors is an exciting advance that could facilitate the development of transgenic mosquitoes that do not transmit malaria parasites.

Research into genetically-modified mosquito strains has concentrated on adding genes that can cause mosquitoes to have immune system reactions to the malaria bacteria. The mosquitoes' own natural defence mechanisms would destroy the disease before the mosquito can pass it on to human beings. If such insects were ever released in the wild, they might supplant infected natural populations helping in the fight against human disease, providing the gm insects are genetically strong enough to supplant a wild and diverse mosquito population.

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New technologies are available that can translate specific genetic sequences into markers or triggers for biological activity such as a new chewing gum to detect malaria. Genetically engineered mosquitoes or other biting insects could deliver minute quantities of vaccine through the saliva every time they bite. More recently, researchers have bioengineered a gene that causes alterations to the mosquito's gut, where malaria parasites incubate. This alteration causes the production of protein that prevents the parasite from binding to the gut walls and could reduce malaria transmission by 80%.

Similarly, in this age of terrorism, genetic engineering could be opening a new way to use insects as bioweapons. It is well documented that insects were systematically explored as a mechanism to spread a variety of diseases during World War II and the postwar US program. Insects can be engineered to produce toxic compounds and deliver them through their natural feeding habit, e.g. in the saliva of mosquitoes. These compounds may exert a broad range of possible effects, from non-life-threatening illness to sterility to widespread fatal illness in a target population. Techniques to use insects to deliver vaccines have already been developed and patented. The development of insect combatants is already a real possibility.

Uganda

At Blackherbals at the Source of the Nile, (UG) Ltd. (BHSN) and the African Traditional Herbal Research Centre (ATHRC), we are committed to finding herbal solutions to the malaria epidemic in Uganda. The use of African traditional medicine in treating malaria is thousands of years old. Yet with all the scientific know-how readily available, there is no real medical breakthroughs and no definitive or economically viable vaccines. Although the West has been able to successfully decipher the human genome and that of the mosquito, it is no closer to bridging the gap between applied theoretical research and practical real-time applications. We are inclined to agree with other African researchers that millions of dollars are being spent on the search for a vaccine that will not be available for years. Thus it becomes a function of economics rather than humanitarian compassion.

Moreover, the practice of pharmaceutical companies isolating a single active ingredient and using it to prepare antimalarial drugs against the parasite and the mosquito has only created more drug resistance and additional side effects. We believe in the traditional holistic approach to disease and the synergetic effects of herbal medicine. The mode of transmission of the plasmodium parasite has been sufficiently determined to effectively allow the use

of herbal plant materials to combat the disease and prevent the infection.

In 2007, the malaria rate in Uganda was 95%. The statistics show that between 30-50 per cent of all outpatients in hospitals, health centres and local clinics were reported malaria cases. Of these, only 20 per cent get admitted, while between 9-14 per cent die of the disease.

Ugandan statistics indicate that one in every two children below 5 years is admitted due to malaria and the disease claims 350 children everyday. Children who suffer acute transmissions can die within a period of 24 hours. Many families spend nearly 25 per cent of household income on treating malaria. Malaria causes the deaths of between 70,000 and 110,000 people annually.

Of over 300,000 malaria cases a year in Uganda, 75,000 are cerebral malaria. Neurological disorders occur when malaria goes untreated. Patients experience symptoms between 10 and 35 days after the mosquito bite. The parasites multiply in the body's blood cells and block the blood's pathway. This leads to a shortage of oxygen and nutrients in the brain, causing neurological disorders and death.

Accordingly, cerebral malaria is the potential cause of epilepsy occurring in tropical areas. Two recent complementary epidemiological approaches were performed in sub-Saharan Africa, in Mali and in Gabon. They were aimed at quantifying the relationship between these two infections. The first one, an exposed/non-exposed study, was performed in a follow-up on Malian children after clinical malaria. Among them, 101 with history of cerebral malaria (CM) were compared with 222 with a history of non-cerebral malaria (NCM). The risk of developing epilepsy was higher after CM than after NCM.

The second approach, a matched case-control study, was performed in a Gabonese population, 6 months to 25 years, at 3 different hospitals in Libreville, going back 15 years. 296 people with epilepsy were compared with 296 people not suffering from epilepsy. The risk of developing epilepsy was higher after CM than in the controls. This work confirmed the role of cerebral malaria in the occurrence of sequela epilepsy.

Gloria's History (Sunday Monitor, Feb 25, 2006)

"Gloria, a 17 year old black female was presented at the African Traditional Herbal Research Clinic in Uganda. At only 7 months of age, Gloria had developed recurrent malaria with no cure. However, it was later discovered that she had also developed cerebral malaria. She suffered various fits whenever her temperatures rose due to

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the fever. In 1990 at only one year, the doctors, after various brain tests, [it was] finally confirmed that Gloria had acquired epilepsy.

Several medical prescriptions were tried and repeatedly failed until an ECG test was performed in 2000 to establish the root cause of the fits. The doctors at Catherine Clinic where Gloria was undergoing diagnosis revealed that her brain-graphing was upside down almost like a short circuit. It revealed that she had high voltage in the forehead, just like a short circuit, mixed waves no clear focus with frequent seizures. The doctor in charge, also the Head of Psychiatrists in Mulago hospital eventually advised the parents to try Butabika Hospital in 2001 for better options since their efforts at the clinic was futile.

It was however, a similar trend of events in Butabika and this led to another referral at the Psychiatric department in Mulago after two years of unrelenting effort. Nonetheless, the parents said, the recommended medications were not only rare and hard to get but expensive as well and despite all this the disease was never cured.

In 2005, the seizures were less violent and Gloria could afford to go to school. She was a happy student, looking forward to sitting her UCE examinations.

However, it was not long before disaster struck in March 2006 and Gloria was rushed to the school dispensary where the personnel there perceived the disease as malaria. According to the parents, improper attention was given to their daughter and her medications were always neglected. By the time they were called in to assess the situation, it was too late and she had to be admitted to another clinic. She suffered a relapse and was consequently paralysed and her vision impaired.

This marked the end of her studies and her dreams of completing O' level and studies altogether. She had to attend physiotherapy in Mulago to restore her ability to walk and feed herself.

The parents described the convulsions as intensely strong and violent. Gloria becomes very stiff, they said, urinates all over herself and sticky saliva constantly drools from her mouth.

She also often bites her tongue and lips and is always in a state of complete unconsciousness. The attacks always come with severe jerking but she can sense them coming hence gets home as fast as possible. They often last about three minutes but can even go up to 30 minutes.

Consequently, Gloria becomes very weak and confused with absolute blackouts. The medicine she was given, the parents said, only serves to lower the violence not frequency such that when they come, which is quite often, all the parents can do is put a spoon in her mouth to prevent her from biting her tongue and lips.

These timeless seizures have had the mother fired from her job because of continuous absenteeism. Her resources were essential in the family's monetary issues.

"All we are looking for is a permanent solution to the disease, a definite cure. It would be laborious to ask for money yet all it would do is find only medicines that control it", the parents said. "We need thorough treatment. If anybody out there has a definite solution, they are very welcome. We want our girl to go back to school, the education she adores," they said."

Herbal Treatment of Malaria and Epilepsy

On March 14, 2007, Gloria was admitted as an outpatient at the African Traditional Herbal Research Clinic in Bukoto, Kampala, Uganda by her parents. She had been hospitalized with malaria, typhoid and epilepsy. She was taking Phenytoin, Folic Acid, Ethosaximide, Tegretol, Panadol, Diclofena, Antidepressants and Zaronin. Since we do not allow any of our patients to take pharmaceuticals while taking herbal products, she was taken off all medications. Gloria was also experiencing stomach pains, painful menstruation every 5 days, and had problems controlling urination. The parents agree to keep a log of her epileptic episodes. She was initially placed on an herbal detoxification and a malaria formulation. She was also given capsicum for only one week.

After nearly two weeks, the treatment included an epilepsy/central nervous system formulation in addition to herbal detoxification and the malaria formula. The patient did not experience an epileptic seizure for one week and her parents said there was much improvement in her condition. Throughout April and beginning of May, the number of epileptic attacks had increased, but the intensity of these seizures had decreased. By the end of April, tests for malaria showed no trace of parasites in her blood and the seizures had diminished drastically by the end of May.

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The malaria formula was discontinued. In June, a blood tonic was substituted for two weeks and detoxification was discontinued but the CNS formula continued throughout her treatment, averaging one 750 ml bottle/week. In June, her seizures had definitely decreased. In July she was given a stronger CNS formulation. Her attacks increased but began to decrease again in August.

In September 2007, Gloria received another ECG test which showed remarkable decrease in the affected area. At this time, she also was also given another Malaria mix for prevention purposes. From November 2007 through January 2008, there were no serious attacks. By March 2008, Gloria had returned to school, was doing well both at school and at home, performing her chores and becoming a good conversationalist. Her parents are very pleased with her progress and to date she is reported to be doing quite well.

Discussion

Traditional Medicine

Traditional medicine is natural plant-based medicine that is more conducive to alleviating the ailments and diseases that affects melanated people. Because plant species evolve and develop naturally as humans do, their natural populations are biologically diverse to the extent that increasing resistance to herbal remedies is not an ongoing problem, as it is presently with pharmaceutical drugs and chemical pesticides created for malaria.

Research studies have shown that the mode of transmission of the plasmodium parasite is through the liver, the blood and other organs. Traditional herbal formulations can be designed to effectively kill parasites in the blood, the liver and other affected organs simultaneously while building the immune system against further attacks. Most western antimalarial products, such as chloroquine, are synthetically designed to interact and use melanin as a carrier, which interferes with the body's natural immune system and diminishes the body's ability to fight the disease.

Hence, even a stressed immune system can trigger a recurring malaria attack. Attacking the parasite on various fronts using the active ingredients in whole plants can naturally reduce the parasite's ability to morph detection in the liver and the blood. There are many active ingredients in the herbal formulations of whole plants which can simultaneously target many systems at the same time, (the synergetic effect), whereas pharmaceutical drugs will employ only one or two synthetic active ingredients.

A survey by Clark et al, 2004 lists 700 taxa associated with malaria and/or fever on herbal plants used in East and Southern Africa. In Uganda, Dr. Tabuti lists at least 27 species used in the treatment of malaria. The most frequently mentioned species were *Vernonia amygdalina* Delile, *Momordica foetida* Schumach., *Zanthoxylum chalybeum* Engl., *Lantana camara* L. and *Mangifera indica* L.

Malaria remains the leading cause of death in Uganda, killing an estimated 320-350 people every day, most of whom are under five years and pregnant mothers. Malaria among children leads not only to illness and death but contributes to their slow development through low birth weight, chronic anaemia, reduced growth and in some cases severe mental retardation. In pregnancy, malaria may cause maternal anaemia, premature births, low-weight babies (which is the principal contributor to infant mortality) and still births. The disease is responsible for nearly 60% of miscarriages in Uganda.

In the past year, Uganda has seen an increase in cerebral malaria cases, which experts at the Malaria Consortium, an international organisation that controls the disease at all levels, are attributing to a shortage of malaria drugs throughout the country. In over 300,000 cases of malaria a year, 25% progress to cerebral malaria. One in nine patients who survive cerebral malaria develops epilepsy. Although 50% of epilepsy cases have had no malaria, the disease is linked to cerebral malaria, especially among children in Africa.

Results

Herbal medicine for malaria in Uganda is shown to be equally more effective, more available and less expensive than western pharmaceuticals. Over 35% of our patients at the African Traditional Herbal Research Centre are presented to us with malaria symptoms. Many of our patients, to include women and children, were previously diagnosed with recurring malaria and laboratory tests continue to show parasites in their blood even after taking western prescription medicines.

Our treatment, a proprietary formula, is taken over a period of 4-6 weeks for prevention. In the four years we have been dispensing this medicine, no one has reported any adverse effects. Laboratory testing of our patients have confirmed the absence of these parasites after treatment and many of them have remained parasite-free for over three years. After three years, an herbal malaria booster is needed. Our formula has been effective in the treatment of acute and chronic malaria even during the onset of symptoms as well as in the prevention of disease. We only use plant species that are endemic to Uganda and thereby making it less expensive and a much more "secure" medicine than western pharmaceuticals.

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In April 2009, our malaria formulation was granted certificate approval by Uganda's National Chemotherapeutic Laboratory (NCRL). Our malaria formula was found to contain alkaloids, tannins, coumarin derivatives, saponins, reducing compounds, anthracenosides, sterols and triterpenes, steroid glycosides, polyuronides, alkaloid salts, anthocyanosides, and flavonosides. Many of these phytochemicals have been found to exhibit medicinal properties. Alkaloids, sterols and tripterpenes, flavonosides, coumarins and tannins have demonstrated anti-bacterial and anti-protozoan properties. The presence of alkaloids imply anti-protozoan activities e.g. anti-malarial.

In an acute toxicity test in rat models, an aqueous ethanol 50% mixture used in young Wistar albino rats shows the formula to be safe and less toxic than chloroquine. There was no toxicity or any significant effect on other systems such as GIT, CVS, Renal, Skin, etc. NCRL's conclusion is that the product is safe for use as presented.

In June 2009, our formulation was presented to the National Drug Authority, so it can be used as an effective alternative to western pharmaceuticals. We are still awaiting approval. Meanwhile, Ugandans are still suffering and dying of malaria.

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Kiwanuka and Nakato Lewis are the owners, the managing directors of RGL Enterprises Intl/BlackHerbals at the Source of the Nile, UG Ltd and www.blackherbals.com and researchers at the African Traditional Herbal Research Centre/Clinic The clinic has been operational for 5 years.

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