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Amazon's Medicinal Plants: A New Solution for Malaria Treatment?

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Editorial

The transmission of *Plasmodium falciparum*, known as being responsible for the lethal and severe form of Malaria, has been importantly reduced in the last few years [1]. However, the effective fight against the disease is still facing some difficulties due to the high capacity of adaptation to the treatment of parasite, increasing its resistance to available medicaments [2]. Indeed, the appearance of *P. falciparum* chloroquine-resistant happened initially in the Magdalena's Valley, Colombia, but soon it was discovered in other Latin America's endemics areas, including Brazil, and Asia. More recently, resistance emerged as well in the African Continent, where it constitutes a stunning problem for disease control. Another relevant fact is the reporting of cases of severe malaria caused by the *P. vivax*, parasite traditionally responsible for the benign form of the disease [3-6].

Interestingly, though malaria is an existing disease since the beginnings of civilization, with reports dating more than 5 thousand years ago, it's systematic treatment only began in the XVII century, when the Jesuits who came to South America observed that plants of the genre *Cinchona spp* (Rubiaceae's family) popularly known as *quinas*, were used for the treatment of febrile diseases. However, only in 1820 the alkaloid quinine was identified as the active substance from Cinchona's barks, becoming the basis of antimalarial therapy since then [7].

Nevertheless, due to quinine`s high toxicity, associated with the appearance of cases of quinine`s resistance, it raised the search for new drugs to treat the disease. New quinoline antimalarials seeking the chloroquine substitution were then synthesized, such as mefloquine, a quinolinemethanol, and halofantrine, a fenantrenomethanol that has schizonticide action similar to chloroquine. Still, mefloquine, a more effective medicine and widely adopted in Asia for the treatment of malaria, is active even in a single dose, but it is toxic and very expensive, in addition to reports of the onset of drug resistance.

In the 80's, a new group of antimalarials come to light, led by artemisinin, extracted from the plant *Artemisia annua*, employed for millennia into Chinese's medicine to treat febrile cases [8]. Semi synthetic artemisinin derivatives, like artemether, artesunate and arteter, are also in clinical use, already. Despite causing rapid clearance of blood parasites, this group of drugs is not able to eliminate parasites and infection might reappear, a phenomenon called recrudescence, being inadvisable their administration as monotherapy. In fact, OMS recommends the "Artemisinin-based Combination Therapy (ACT)" for malaria treatment, worldwide employed for the fight against *P. falciparum* chloroquine-resistant, comprising the combination of artemisinin derivatives with antimalarials, such as mefloquine, lumefantrine, and others [7].

On the other hand, as feared, the reduction of *P. falciparum* response to monotherapy with artemisin was reported in 2012, and resistance is well established on Camboja's and Thailand's border [9].

Therefore, there is a consensus that the investigation of new antimalarial drugs is urgent. According to this, plants commonly utilized for malaria treatment can give valuable contribution [10].

Into Brazilian's Amazon a large number of vegetables are routinely utilized for the treatment of febrile and malarial diseases. All this "inlander medicine" was inherited from the Indians, first habitants of this region, with the addition of African and European contributions, too. However, mostly of these plants have no studies that assess their antimalarial activity, toxicity and other relevant aspects [11]. Going through the same way, some ethnobotanical studies in the Brazilian's Amazon describe the ordinarily use of plants for malaria treatment and/or febrile diseases, highlighting Apocynaceae, Asteraceae, Leguminosae, Rhamnaceae, Iridaceae, and other families. In order to validate this traditional use, our research group is systematically evaluating antimalarial activity (against *P. falciparum and P. berghei*) of Amazonian plant species with popular claim for malaria and febrile diseases. A significant number of species have displayed *in vitro* and *in vivo* antiplasmodial activity. In general, the most promising species were those rich in alkaloids and quinines [11].

Among the species evaluated up to the moment, the most promising is *Eleutherine plicata* (Iridaceae), in which high antiplasmodial activity was identified without significant increase of cytotoxicity. Studies in *P. berghei* infected mice treated with ethanolic extract from the barks of the plant showed a significant reduction of parasitemia, as well as of parameters of oxidative stress associated with the disease.

However, much is still needed in order to obtain therapeutic drugs from the extracts of this plant. Nevertheless, the therapeutic potential of Amazon's plants is still a universe that, if properly explored, will lead to the development of more effective drugs for the treatment of malaria and many other diseases of today.

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